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ORGANIC CHEMISTRY

INCLUDING CERTAIN PORTIONS OF

PHYSICAL CHEMISTRY

FOR

MEDICAL, PHARMACEUTICAL, AND BIOLOGICAL
STUDENTS

(WITH PRACTICAL EXERCISES)

✓ BY

HOWARD D. HASKINS, A.B., M.D.

*Associate Professor of Organic Chemistry and Bio-Chemistry,
Medical Department, Western Reserve University.*

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SECOND EDITION

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PREFACE TO SECOND EDITION.

THE author has endeavored to revise the entire book, striving to make it more reliable as a reference book, and more complete from the standpoint of the student of medical sciences. It is our belief that an organic chemistry text-book for the use of medical students should give the chemistry of all the organic compounds (of any importance) that enter into the study of physiology, biochemistry, and pharmacology.

H. D. HASKINS.

July 1, 1912.

PREFACE TO FIRST EDITION.

AMONG the most important of the recent advances in medical science are those relating to the chemistry of the various organic substances which enter into the composition of animal tissues and fluids, and to the physico-chemical laws which govern, or at least influence, many physiological processes. The discovery of the chemical constitution of the purin bodies, of many of the urinary constituents, and of sugars and fats, as well as the new theories of solution and catalysis, has revolutionized the teaching of biological and clinical chemistry; and in pharmacology and pharmacy a knowledge of organic and physical chemistry is almost essential. The study of these parts of chemistry is, therefore, daily coming to be of greater importance to the medical student and is already included in the curriculum of the best medical schools.¹

As taught in the regular college classes in organic chemistry, the subject certainly absorbs too great a

¹The recent application by Arrhenius of certain physico-chemical laws in explaining the mode of action of antitoxins, etc., is an illustration of the increasing importance of a knowledge of physical chemistry for the medical student.

proportion of the medical student's time, and much is included in the course which has no bearing on his future work, and much is omitted which is of immense importance to him.

It was with the idea of presenting in the simplest manner the facts of organic and physical chemistry which have an essential bearing on medical science that the present book was written. For the sake of simplicity, the subject-matter is arranged in a somewhat different manner from that usually followed in text-books for chemical students. In the first portion of the book considerable attention is given to a description of the methods employed for purifying and testing the purity of substances preparatory to their further investigation. It is to this part of his work that the investigator in bio-chemistry has to give his closest attention and in which he often meets with the greatest difficulties. A chapter giving a fairly full description of the methods of elementary analysis follows, and then a chapter on the principles of physical chemistry as applied to molecular weight determinations and to the theories of osmosis, solution, etc. Those facts of physical chemistry which it is desirable to call attention to that are not included in this chapter are inserted where they can most conveniently be studied along with the organic compounds. The remainder of the book includes a description of the various groups of organic substances, and, where possible, there is chosen, as the representative of each group, some body of medical or biological importance. Numerous practical exercises accompany the text, and these have been chosen and arranged so as to occupy about four

hours of laboratory work per week for a thirty-week session. A few more advanced exercises are given for the sake of completeness, and it is left to the teacher whether or not he shall have them performed by the student. The cyclic compounds and the more complicated of the benzene derivatives may also be omitted at the discretion of the teacher.

In the Appendix will be found a schedule showing how the work of the class in our own institution is arranged so that all the members of it may do those experiments involving the use of expensive apparatus. The laboratory work is required of our students. We believe that by conducting an elementary analysis and by doing cryoscopic experiments with Beckmann's apparatus, as also by preparing pure organic compounds, the student acquires an idea of accuracy and an insight into the principles of chemical methods which he cannot otherwise obtain, and which, without any doubt, will be of immense value to him in all his future work. Our experience is, also, that students of whom laboratory work is required get a grasp and understanding of the subject of organic chemistry such as others rarely acquire.

H. D. HASKINS.

J. J. R. MACLEOD.

April, 1907.

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ORGANIC CHEMISTRY.

CHAPTER I.

THE NATURE AND COMPOSITION OF ORGANIC COMPOUNDS.

Definition of Organic Chemistry. The various inorganic chemical compounds are classified by the chemist into groups, a group comprising all the compounds of some particular element. Thus we have the iron group, the sulphur group, and so on. On account, however, of the great number¹ of compounds containing the element carbon, the group of carbon compounds is set apart for consideration as a special branch of chemistry. Organic chemistry is that branch: *it is the chemistry of carbon compounds*. This definition is, however, not strictly accurate, for it is customary to treat of the oxides of carbon and the carbonates in inorganic chemistry.

The name organic owes its origin to the old-time belief that these compounds of carbon could be produced only by the agency of vegetable or animal organisms, by so-called vital activity. That such a notion

¹ Over 112,000.

is untenable was first shown by Wöhler, who, in 1828, obtained urea—the main organic constituent of urine—by simply evaporating an aqueous solution of ammonium iso-cyanate, his intent being to recrystallize the latter salt (p. 224). Since that date thousands of organic compounds have been prepared in the laboratory without any assistance from vital processes. In fact, a great proportion of the compounds known to organic chemists have never been discovered in nature, but have been created in the chemical laboratory.

Elements and their Detection. In organic compounds carbon may exist in combination with one, two, three, four, or even five other elements. The most important elements present in organic compounds, together with their atomic weights and valences, are as follows:

Carbon,	C.....	atomic wt. 12,	valence IV.
Hydrogen,	H....	“ “ 1,	“ I.
Oxygen,	O...	“ “ 16,	“ II.
Nitrogen,	N...	“ “ 14,	“ III and V.
Phosphorus,	P....	“ “ 31,	“ III and V.
Sulphur,	S.....	“ “ 32,	“ II, IV and VI.

Some important compounds contain the halogens (Cl, Br, I). The presence of most of these elements in organic compounds can be quite readily detected by simple tests, the principal ones being incorporated in the experiments that follow. The presence of oxygen cannot be directly determined; it is detected by finding the percentage composition of the compound and observing that the sum of the per cents of all the other elements is less than one hundred.

EXPERIMENTS. Detection of carbon, hydrogen, nitrogen, sulphur, and phosphorus.

(1) **C** and **H**. Dry a clean test-tube in the gas-flame. Fit it with a cork through which passes a glass tube bent at a right angle. Mix in a mortar a little dry cane sugar and ten times as much dry CuO , pour this mixture into the test-tube, cork, and dip the outside end of the glass tube into baryta solution contained in another test-tube. Heat the sugar mixture over a flame. Drops of water condense on the cool parts, showing the presence of **H**.¹ Cloudiness in the baryta is due to carbon dioxide, forming BaCO_3 , and indicates the presence of **C**. By heating CuO it is reduced; its oxygen combines with the **C** and **H** of the organic substance to produce CO_2 and H_2O .

(2) **N** and **S**. (a) Triturate in a mortar some dry albumin with twenty times as much soda-lime,² transfer the mixture to a test-tube, and heat over a flame. Test the vapour that appears for ammonia, the presence of which proves the existence of **N** in the compound examined.

(b) Put into a dried test-tube some dry albumin equal in bulk to a bean. Add a small piece of clean metallic sodium. Heat until the mass is red-hot, then *gently* drop the test-tube into a small beaker containing 10 c.c. of distilled water. The tube breaks, and NaCN and Na_2S go into solution. Filter and divide the filtrate into portions *A*, *B*, *C*, and *D*. To *A* add NaOH

¹ Water of crystallization must be removed before testing for hydrogen.

² Soda-lime is made by gradually adding powdered quicklime to a saturated solution of caustic soda with constant stirring.

until strongly alkaline, then a few drops of freshly made FeSO_4 solution¹ and a drop of Fe_2Cl_6 solution. Boil this mixture two minutes, cool, and acidify with HCl . The appearance of a greenish-blue colour or a precipitate of Prussian blue indicates N. To *B* add a few drops of a *fresh* solution of sodium nitroprusside;² a reddish-violet colour points to the presence of S. To *C* add lead acetate solution and acidify with acetic acid. A brownish-black discoloration or precipitate is due to S. Neutralize *D* with HCl ; add a few drops of Fe_2Cl_6 solution: a red colour, which is removed by HgCl_2 , is caused by the presence of sulphocyanide.

If sulphocyanide is not formed in examining an organic compound by this method, halogens may be tested for in the filtrate by boiling some of it with one-tenth volume of concentrated HNO_3 (HCN or H_2S driven off—prolonged boiling may be necessary to remove all the HCN) and then testing with AgNO_3 (precipitate of AgCl , AgBr , or AgI). In this test iodine and bromine are set free by the nitric acid and can be detected by odour and colour.

If it is desired to detect N, S, or halogens in a liquid it is best to drop the liquid on to melted sodium contained in a test-tube which is held vertically by being thrust through a hole in an asbestos pad.

(3) **P.** Mix some dry nucleoprotein (or dry yeast) with twenty parts of fusion mixture (1 part Na_2CO_3 + 2 parts KNO_3). Heat in a crucible until the mass is almost white. When cool, dissolve it in a little hot water and pour the resulting solution into an evaporating dish. Add HCl until neutral and filter. To half of

¹ Sodium ferrocyanide is formed by this treatment.

² Formula = $\text{Na}_2\text{Fe}(\text{CN})_6(\text{NO})$.

the filtrate add NH_4OH until strongly alkaline, then add magnesia mixture.¹ The phosphates, formed by the oxidation of the phosphorus of the compound, cause a white precipitate. To the other half of the filtrate add HNO_3 until strongly acid, then add an equal volume of ammonium molybdate solution² and heat in a water bath until a *fine* yellow precipitate appears.

Having thus determined what elements are present in the organic compound that he is investigating, the chemist next proceeds to its more thorough examination. He first estimates the percentage amounts of the various elements contained in the substance, and then he determines its molecular weight. He is able from these data to calculate the empirical³ formula. But more than one substance may have this same formula; therefore he studies the reactions of the compound when treated with reagents in order to get a clue as to how its molecule is built up, that is, how its atoms are linked together. And, finally, by causing simpler substances, the structure of whose molecules is known, to become united (*synthesis*), he endeavours to produce a substance having the same molecular structure as his compound.

¹ Magnesia mixture is made as follows: Dissolve 55 gm. of pure MgCl_2 crystals and 70 gm. NH_4Cl in 1300 c.c. of water and add 350 c.c. of 8% ammonium hydroxide.

² Ammonium molybdate solution is made as follows: Dissolve 75 gm. ammonium molybdate in 500 c.c. of water and add 500 c.c. of HNO_3 of specific gravity 1.2.

³ The empirical formula gives merely the total number of atoms of each element in one molecule, as $\text{C}_6\text{H}_{12}\text{O}_6$ (see p. 76).

If his synthetic compound shows properties that are identical with the substance under examination, the chemist then considers that he has established with absolute certainty the chemical construction of the compound.

But all this work will end in failure unless the substance under examination be absolutely pure, i.e., free from admixture of any other substances. It is necessary for us at this stage, therefore, to explain the chief methods of purification as well as the tests by which the purity of the substance is ascertained. This will be done in the chapter that follows.

CHAPTER II.

PURIFICATION AND IDENTIFICATION OF SUBSTANCES.

PURIFICATION OF SUBSTANCES.

THE main methods of separating an organic substance in a pure state are *crystallization*, *sublimation*, *distillation*, and *dialysis*.

Crystallization. The basis of this method is the fact that different substances are not usually soluble to an equal extent in the same solvent. For example, acetanilide can be separated from dextrose by dissolving the mixture of these two in hot water: on cooling the resulting solution, the acetanilide crystallizes out because of its slight solubility in cold water, while the dextrose remains in solution. By repeated crystallization in this manner perfectly pure acetanilide can be obtained (see exp. below).

Inasmuch as crystallization as a method for separation and purification of organic compounds is invaluable, it will be well to detail specific directions for carrying it out. (1) Carefully select a suitable solvent. Put small quantities of the substance to be purified into several test-tubes; add to each a different solvent—those most commonly used are water, alcohol, ether, chloroform, benzol, petroleum ether, acetone, and

glacial acetic acid. Discard those which dissolve the substance readily. Heat each of those that remain. Choose the solvent which when hot dissolves the substance readily, but deposits crystals on cooling. The solvent should either hold the impurity in solution when cold or exert no solvent action on it whatever.

(2) Completely saturate at boiling temperature a certain quantity of the chosen solvent with the substance.

(3) Filter the hot liquid through a plaited filter, using a funnel with a short stem. (With a long-stemmed funnel crystals may separate out in the stem and block it.) Heating the funnel in hot water before filtration may be resorted to.

(4) Collect the filtrate in a beaker having a capacity twice the volume of the liquid. With too small a beaker creeping of crystals and liquid may occur.

(5) Cool slowly.¹ If crystals are deposited very quickly, redissolve with the aid of heat, and prevent rapid cooling by wrapping the beaker with a towel.

(6) Cover the beaker with a piece of filter-paper to prevent condensation-drops falling back into the liquid and disturbing the crystallization. A watch-glass or glass plate completes the covering.

(7) Do not disturb the beaker until crystals have formed. If their appearance is greatly delayed they may often be induced to form by scratching the inner wall of the beaker with a glass rod, or by "sowing" a crystal of the substance into the liquid.

(8) If the substance is not sufficiently insoluble in

¹ 5, 6, and 7 may be disregarded except when the form of the crystals is to be studied.

the cold solvent, crystallization may be brought about by slow evaporation in a wide crystallization dish which is loosely covered, as with fractional crystallization.

(9) Collect the crystals on a suction-filter (reject the crystals that have crept above the surface of the liquid), wash them with a little of the pure cold solvent.

(10) Dry the crystals in a desiccator, except when they contain water of crystallization.

EXPERIMENT. Put 20 c.c. of distilled water into a beaker and heat to boiling on an asbestos pad. Completely saturate it with the mixture of dextrose and acetanilide which is furnished. Filter while hot, and cool rapidly. When a good crop of crystals has formed, separate them by filtration. Dissolve and recrystallize. Repeat the process until the filtrate from the crystals no longer reduces Fehling's solution.¹ At least three crystallizations should be carried through. Save the pure white crystals. After drying them in a desiccator a determination of the melting-point may be made (see below).

To test the purity of the crystals their melting-point is determined. The method of making a melting-point determination will be described in the experiments that follow. Pure crystals melt quite sharply and completely, i.e., they become completely melted within 0.5° to 1° . The crystals may be considered pure when,

¹ Fehling's reagent consists of an alkaline solution of cupric hydroxide, the latter being held in solution by means of Rochelle salt. The reagent is of a deep-blue colour, and when it is boiled with even a trace of dextrose a red precipitate forms in it.

after repeated crystallization, the melting-point remains constant for several successive determinations. A bath of water may be used for substances having a low melting-point (below 80° ¹). Sulphuric acid is used for higher temperatures (up to 280°). For still higher temperatures paraffine is used. The thermometer should be one with the scale engraved on the stem. The crystals should be powdered and thoroughly dried in a desiccator.

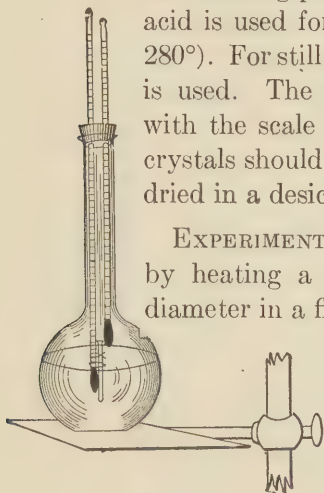


FIG. 1.

EXPERIMENT. Make melting-point tubes by heating a small glass tube of 4 mm. diameter in a flame until red, then suddenly drawing it out. A capillary tube about 1 mm. in diameter is thus obtained. Break into lengths of 6–8 cm. and seal one end of each. Put into such a tube some powdered chloral hydrate which has been dried in a desiccator. Gentle scratching with a file will cause the particles to travel to the bottom of the tube. Attach the tube to a thermometer by means of a narrow rubber band cut off from rubber tubing, adjusting it so that the main part of the chloral will be opposite the middle of the bulb of the thermometer. Suspend the thermometer in a beaker of water so that the bulb is fully immersed. Heat the water very gradually. Note the temperature at which there is the first indication of melting (beginning transparency or collapsing

¹All temperatures given in this book are centigrade.

against the wall of the capillary tube of any portion of the crystalline substance) also the temperature of actual fusion.

Into another capillary tube put pure dried powdered urea;¹ attach the tube to a thermometer with a fine platinum wire, adjusting it as above. The bath in this case should be pure H_2SO_4 containing 30% of K_2SO_4 (to lessen fuming), contained in a long-necked Jena flask (as, for example, a Kjeldahl incineration-flask). By means of a loosely-fitting cork suspend the thermometer in the flask, with its bulb dipping into the bath. In a similar manner suspend another thermometer to take the temperature of the air above the H_2SO_4 . Heat gradually. When melting occurs, place the bulb of the second thermometer midway between the meniscus of the mercury in the stem of the first thermometer and the surface of the bath; from this quickly make the reading of the air temperature (this is t in the formula below). Also measure in degrees the height of the mercury column above the surface of the H_2SO_4 ($=L$ in the formula). *The correction which must be added* to the observed reading (which is T) on account of the stem of the thermometer and mercury thread being cooler than the bulb can be calculated by the formula: $L(T - t)(0.000154)$.² The corrected³ melting-point of pure urea is 132.6° .

¹ Where "pure urea" is called for it is best to prepare it by recrystallizing some urea from hot absolute alcohol.

² The coefficient of expansion of mercury in glass is 0.000154.

³ The melting-points marked "corrected" are quoted from *H. Meyer's Analyse und Konstitution der organischen Verbindungen*.

For the most accurate work in determining melting-points careful attention to a number of things is essential. Tested thermometers of a standard thickness should be used. A set of thermometers of limited range, as $0-50^{\circ}$, $50-100^{\circ}$, $100-150^{\circ}$, graduated for 0.2° , would be desirable. The melting-point tube should have about the same thickness of wall as the wall of the bulb of the thermometer.

The crushed crystals should be sifted through a fine mesh screen, as variation in size of the particles gives variation in melting-point. The tube should be filled for only about 3 mm. of its length, solidly packed. The initial heating may be rapid until a temperature 20° below the melting-point is reached, then the heating should be such as to cause not over 3° rise per minute, and near the melting-point 0.5° per minute. Stirring of the bath is desirable. A double bath by means of which the air about the thermometer is heated as well as the liquid insures greater accuracy. Such an apparatus can be constructed by taking a tall Jena beaker (17-20 by 8 cm.) and suspending in it a large test-tube (20×3 cm.). Pour into the test-tube alboline (liquid vaseline) to a depth of 5 cm., and fill the beaker for nine-tenths of its depth with the same liquid. As a stirrer use a piece of gold-plated wire, coiled in a large spiral at the end to fit loosely the inside of the test-tube. Suspend the thermometers in the test-tube as shown in Fig. 1. When approaching the melting-point, stir steadily. An air temperature of only $3-7^{\circ}$ below the oil temperature is secured, hence it is unnecessary to calculate a correction.

A method of purification applicable to certain solid substances is **sublimation**. A substance sublimes when it passes readily from the solid state to a vapour. The method is carried out as follows. A watch-glass or evaporating dish containing the substance is covered with filter paper which has several pin-hole perforations. A funnel which is of a size to fit neatly is inverted over this, the stem being loosely plugged with cotton

The dish is heated gradually until vapour passes into the upper chamber of the apparatus and condenses on the cool walls of the funnel (see exp., p. 321).

Distillation. This method is useful mainly for the purification of liquids. Certain solid substances, however, can be distilled to advantage. When the impurity is a material that will not vaporize at the temperature employed (i.e., at a temperature at which the substance itself readily vaporizes), simple distillation suffices.

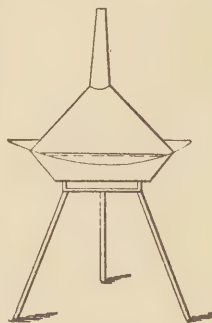


FIG. 2.

When, however, a mixture of volatilizable liquids is dealt with, fractional distillation has to be resorted to. This method is described in the following experiment. Certain mixtures cannot be resolved into their constituents in the pure state by fractional distillation, such as a mixture of water and alcohol, or methyl alcohol and benzol.

EXPERIMENT. Set up a distillation apparatus as shown in the diagram. Into the fractionating flask—a flask having a branch tube fused into the neck as a delivery-tube for the vapour—pour through a funnel about 300 c.c. of 50% alcohol, and drop in a couple of capillary tubes. Select a cork that will fit the flask tightly. Through a hole in the cork insert a thermometer, and hang it so that the bulb is in the stream of vapour, i.e., opposite or below the opening of the side tube. The bulb must not be below the neck nor low enough to be splashed by the boiling

liquid. Heat on a water bath. Have four clean dry receiving flasks ready and labelled. In the first flask collect all the distillate coming over while the thermometer registers a temperature between 78° and 83° . Now dry the outside of the fractionating flask with a cloth and change it to an asbestos pad having a hole one inch in diameter. In the second flask collect that distilling between 83° and 88° . Flask number three

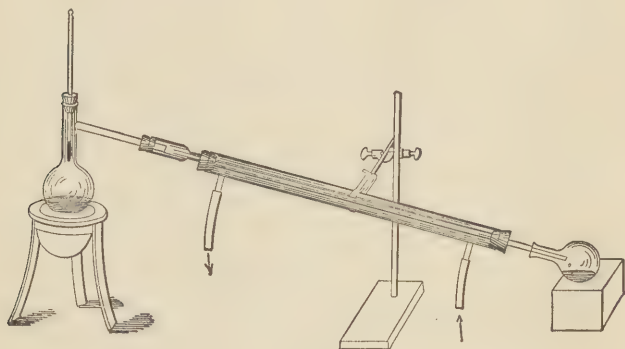


FIG. 3.

is to catch the distillate between 88° and 93° . The last flask receives all that distils over above 93° . (Do not distil over all the water.) Measure the amount of each fraction, and of the residue in the flask. Drain and dry the condenser tube.

For the second distillation use a smaller fractionating flask or a small flask with a bulbed column attached as shown in the diagram. Pour into it the fluid in flask number one and use the latter as the first receiving flask for the distillate. When the temperature reaches 80° pour the contents of flask number two into the fractionating flask, and when the temperature again

rises to 80° replace flask number one by flask number two as the receiver, also change the distilling flask to the asbestos pad as before. When the temperature reaches 83° add the liquid in flask number three to the fractionating flask, and distil until the temperature reaches 88° .

Determine the per cent of alcohol in these three fractions by taking the specific gravity of each with Westphal's balance (see p. 21), and comparing with the table (p. 403). By repeated fractionating practically all of the alcohol is

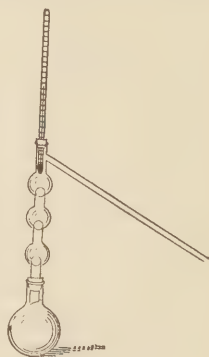


FIG. 4.

brought into flask number one and most of the water into flask number four. As, however, it is simply the alcohol that is of value in this case, redistil the first fraction only and secure a distillate coming over at $78-79^{\circ}$, this should contain at least 90% (by volume) of alcohol.

Distillation is sometimes carried out by bubbling steam through the mixture, which is kept at a temperature of at least 100° . By this means substances which boil even above 200° can be obtained in the distillate, mixed, of course, with a large quantity of water (see Fig. 5). (Compare phenol, p. 303).

Vacuum distillation is employed in certain cases, particularly when it is desirable to lower the boiling-point in order to prevent any decomposition of the substance. Many substances decompose at a temperature below their boiling-points. The distilling apparatus is closed up air-tight except for a finely pointed tube which dips below the surface of the heated liquid

and, passing through the stopper, is open to the air: through this tube fine bubbles of air keep the contents of the flask in commotion and prevent bumping. The receiving flask is connected with a suction-pump. A

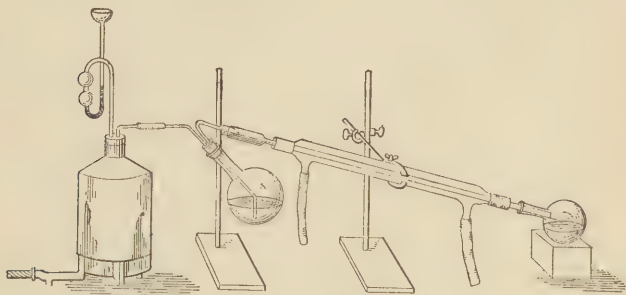


FIG. 5.

reduction of pressure in the apparatus to 30 mm. of mercury (atmospheric pressure being about 760 mm.) will usually lower the boiling-point of a high-boiling

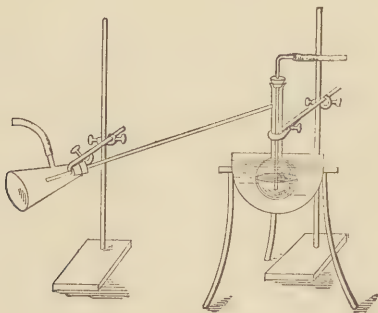


FIG. 6.

substance by nearly 100° . An ordinary suction-pump is usually quite satisfactory for lowering the pressure (see fig. 6).

The test of purity of a substance that distils is constancy of boiling-point. If, after repeated fractional distillation, a material is obtained which has the same boiling-point each time and which distils over completely at that temperature, it is most likely a pure substance.

EXPERIMENT. The boiling-point flask should be either a long-necked fractionating flask which has the side

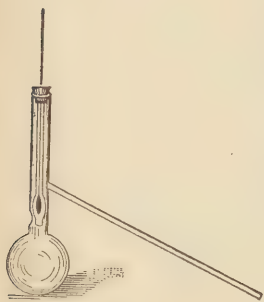


FIG. 7.

tube coming off very high up near the cork, or an ordinary fractionating flask into whose neck is fitted an open tube slightly expanded at the lower end so as to fit the neck, while the latter has been dented with a blast-flame at the proper point to prevent the tube slipping into the chamber of the flask (see fig. 7). In such an apparatus the vapour passes up to the cork, then

descends outside the tube, heating the stem of the thermometer for the whole length of the mercury column, the thermometer being lowered sufficiently to permit this.

The thermometer used should be of the same kind as those specified for melting-point determination (p. 12).

Put 20 c.c. of pure chloroform into the flask; support the flask on wire gauze (it is advisable to interpose between the gauze and the flask an asbestos pad having a hole one inch in diameter). Attach a long tube as an air-condenser and place a receiving flask in position. Heat with a small flame. When vapour passes freely into the condenser, note the temperature.

Continue distillation until the temperature has remained constant for at least five minutes. Take the reading as the boiling-point. No correction is necessary except for barometric pressure. This correction can be calculated approximately by adding to the observed boiling-point 0.038° for each mm. below 760 mm. barometric pressure or subtracting 0.038° for each mm. above this¹. The boiling-point of chloroform at 760 mm. pressure is 61.2° (corrected)².

The author has devised a simple apparatus by which the boiling-point can be determined under standard pressure, avoiding calculation of a correction.³

The special distilling flask (Fig. 7) is connected with an air-tight condensing apparatus, a filtering flask (as receiver) being fitted onto the end of the condenser. The side tube of this flask is connected with tubing containing air under pressure, coming from the blower part of a large Wetzal suction pump. A calcium chloride tube or tower is interposed, to prevent moisture getting into the flask. The compressed-air system is connected also with a barometer (or with a second distilling apparatus, as suggested below) of the older type which is bent in U form at the bottom; and furthermore is connected with a tube that is suspended in a tall cylinder of water. By raising

¹ If the boiling-point is around 100° the factor of correction is 0.044, if 150° it is 0.05, if 200° it is 0.056 and 250° it is 0.062. For water, alcohol, organic acids, and other liquids whose molecules become associated (p. 60) the figures are lower: around 50° it is 0.032, 100° it is 0.037, 150° it is 0.042, 200° it is 0.046 and 250° it is 0.051.

² The boiling-points marked "corrected" in this book are those given in *Traube's Physico-chemical Methods*.

³ Smith and Menzies have recognized the desirability of securing the boiling-point at this standard pressure. They recently (1910) described an apparatus for the purpose. Their method, however, makes use of a small boiling-point bulb which is tied to a thermometer, and is submerged in a bath.

or lowering this tube, the pressure in the distilling apparatus as recorded by the barometer can be brought to any height which could occur as atmospheric pressure. It must be remembered that a small correction of the barometer must be made for the temperature, since standard barometric pressure is 760 mm. when the mercury of the barometer is at 0° . For example, if the temperature of the room is 15° , the apparent pressure in the apparatus must be 762 mm. (glass scale, 761.9 mm. if brass scale), in order to get the boiling-point under 760 mm. pressure.

The apparatus can be used to demonstrate the amount of change of boiling-point for definite changes of pressure.

After accurately determining the boiling-point of an absolutely pure liquid which is stable and not inclined to absorb moisture (as benzene), the apparatus can be arranged to eliminate the barometer by connecting a second air-tight distilling apparatus in which to boil the liquid that is under examination. Now regulate the pressure so that the liquid of known boiling-point distils at a temperature corresponding to standard pressure as previously determined (read to 0.1°), then the temperature at which the other liquid distils will be the boiling-point of the latter at 760 mm.

If the liquid has a high boiling-point shield the flask with a metal or asbestos cylinder that rests on the asbestos pad.

Dialysis is occasionally employed for purification purposes, especially in bio-chemistry. It depends on the well-known fact that crystalloids can diffuse through animal membranes or parchment paper, whereas colloids cannot. Thus, to separate sodium chloride from egg proteid a solution containing these is placed in a dialyser suspended in pure running water: the sodium chloride diffuses out, leaving the egg proteid in the dialyser.

IDENTIFICATION OF SUBSTANCES.

When the substance has been purified by the above methods, identification may be attempted. For this

purpose its *physical properties* are studied; its colour, odour, and taste are carefully noted, and determinations are made of its melting-point, boiling-point, crystalline form,—including measurement of the angles of the crystals,—density or specific gravity, action on polarized light, spectroscopic appearance, refractive power, and solubilities. The data thus obtained are compared with those of known substances.

Next to the first five properties mentioned, the most universally useful one for purposes of identification is specific gravity. The method of determining this we will describe here. Those of the other properties not already described will be found in one or another of the larger laboratory manuals.¹

The specific gravity of liquids may be found by several different methods. 1. The weight of equal volumes of the liquid and of water may be successively



FIG. 8.

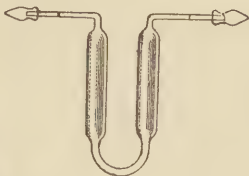


FIG. 9.

determined in a special stoppered bottle called a *picnom-*

¹ *Gatterman*. The Practical Methods of Organic Chemistry. Translated by Schober.

Mulliken. Identification of Pure Organic Compounds.

Lassar-Cohn. Laboratory Manual of Organic Chemistry; also, Arbeitsmethoden für organisch-chemische Laboratorien.

eter. The temperature of both fluids at the moment of weighing must be reported. The temperature of the water taken as the standard for comparison may be 0° , 4° , or 15° . The most convenient form of pycnometer is one which holds exactly 10, 25, or 50 gm. of pure boiled water at 15° (see fig. 8). Further details are explained in the experiment below.

2. *Westphal's balance* is a very useful instrument for finding specific gravity (see fig. 9). Riders of different sizes are used on this balance, each one representing a different decimal place in the specific gravity. This instrument gives the specific gravity of the liquid at the temperature of observation compared with pure water at 15° .

3. The *hydrometer* is another empirically graduated instrument for determining specific gravity, water at 15° being the standard. It is a glass float having a long stem; this sinks in the fluid, so that the surface comes to a certain mark on the stem, and the figures which are read off at that mark indicate the specific gravity (see fig. 10).

The urinometer is a hydrometer for use with urine.

The specific gravity of a solid can be found by weighing it in the air, then reweighing it while immersed in water. This method has very little application in organic chemistry. The specific gravity of crystals or small solids can be determined by placing an accurately weighed quantity of them in a pycnometer filled with some liquid in which they are insoluble (see exp. below).



FIG. 10.

EXPERIMENTS. (a) *Specific gravity of petroleum ether.* Weigh accurately an empty dry picnometer which will hold just 25 gm. of pure water at 15°; deduct from the weight 0.027 gm. for the weight of the contained air. Remove the stopper and fill with petroleum ether (boiling at 60–70°). Wrap a strip of folded filter-paper about the neck to catch the overflow, insert the stopper so that no air is left in the bottle, wipe off gently, and reweigh. When weighed, note the temperature as indicated by the thermometer in the stopper, also make sure that no air has been drawn into the bottle by cooling and consequent contraction of the fluid. The difference between the two weights gives the weight of the petroleum ether, and this divided by the weight of an equal amount of water (25 gm.) gives the specific gravity as compared with water at 15°. In recording specific gravity report the temperature of observation; for example, petroleum ether $S_{15}^{18} = 0.7$ means that the specific gravity of petroleum ether at 18° is 0.7 when compared with water at 15°. Also determine the specific gravity of the ether with the Westphal's balance.

(b) *Specific gravity of urea.* Weigh a little test-tube which contains pure dry urea crystals. Remove the stopper of the picnometer used in (a); pour the urea into the petroleum ether. Tap the picnometer to cause the air adhering to the crystals to be dislodged. Now fill the neck with more petroleum ether, insert the stopper as before, and reweigh. The petroleum ether must be at the same temperature as in (a). Reweigh the urea tube; by deducting this weight from the previous one find the weight of the urea in the picnometer.

To find how much petroleum ether has been displaced by the urea (the latter being insoluble in the former) add to the weight of the bottle filled with petroleum ether (exp. *a*) the weight of the urea, then deduct from this sum the weight of the bottle containing urea immersed in petroleum ether (*b*); the difference is the weight of the petroleum ether displaced. Divide this by the specific gravity of petroleum ether; the result indicates the displacement in cubic centimetres, or rather the weight (in grams) of an equal quantity of water, so that the weight of the urea used divided by this figure gives the specific gravity. The specific gravity of urea is about 1.33.

If the substance under investigation is known to chemists it can generally be identified by comparing the data gathered as to its properties with tabulated lists¹ of boiling-points, melting-points, specific gravities, etc. Generally an accurate determination of the boiling- or melting-point and of the specific gravity will definitely locate the substance. When dealing with a liquid it is advisable, if there exists any doubt about the nature of the substance, to determine the specific gravity at several different temperatures. When relying on melting point for identification it is of value to bear in mind that two different substances may have nearly the same melting-point, but a mixture of them melts at a far different temperature. Therefore, mix some of the

¹Such tables may be found in *Physikalisch-chemische Tabellen* by *Landoldt and Börnstein*, *Chemiker-Kalendar* by *Biedermann* (yearly editions), *Melting and Boiling Point Tables* by *Carnelly*.

known substance with that which is supposed to be identical with it and determine melting-point; if this is the same as for the unknown substance, then identification has been completed.

If the substance is still unknown or cannot be positively identified, an accurate analysis is made to determine the percentage by weight of each element present in it.

CHAPTER III.

ELEMENTARY ANALYSIS.

The estimation of the carbon and hydrogen present in a compound is made by combustion in the presence of cupric oxide, the end-products of combustion being carbon dioxide and water. The method is in principle exactly the same as that for the detection of carbon and hydrogen.

The combustion is carried out in a glass tube of difficultly fusible glass having an inside diameter of about 1.5 cm. This tube should be 10 cm. longer than the furnace in which it is to be heated—85 cm. is a good length. A tube of this length is charged for combustion as follows: a short roll or spiral of copper gauze is inserted and pushed in 5 cm. from the end, moderately coarse cupric oxide (of wire form) is poured into the other end until it occupies 35–40 cm. of the tube next to the spiral, then another short copper spiral is pushed down to the coarse oxide to hold the latter in place, the next 20 cm. of the tube is occupied by the substance to be analyzed mixed ¹ intimately with fine cupric oxide

¹ The substance may be placed in a little platinum or porcelain boat instead of being mixed with CuO. If a liquid is to be analyzed it is sealed in a little glass bulb, and this is placed in the combustion-tube.

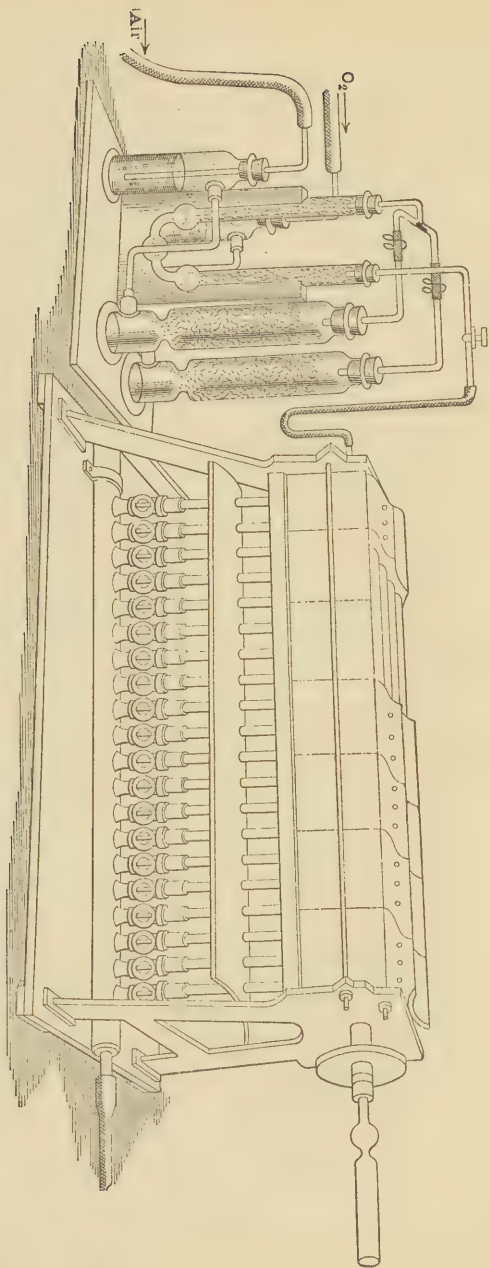


Fig. 11.

(wire form) in the manner described in the experiment below, then follows a short copper spiral (which has a wire loop attached) and finally some coarse cupric oxide. Each end of the tube is closed with a rubber stopper. Through the stopper at the end nearest the fine oxide mixture passes a glass tube which is connected with the apparatus for purifying the incoming air or oxygen.

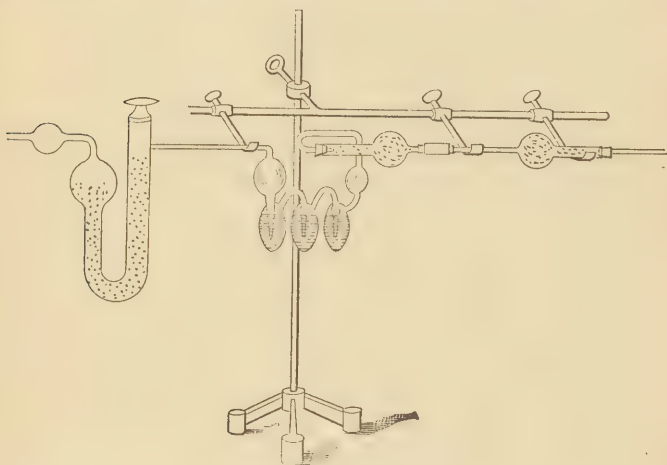


FIG. 12.

The absorption apparatus which collects the products of combustion is connected directly with a glass tube passing through the stopper at the other end.

When a tube is in service for the first time, to insure complete removal of any organic matter that might be clinging to the glass or the copper oxide, the fine oxide is used unmixed with any other substance, and the whole tube is heated for several hours while a stream of dry air is passing through. In this case an ordinary

calcium chloride tube takes the place of the absorption apparatus. If moisture has collected in the tube toward the end it must be removed by warming the tube at that point. A stream of air can be used for the combustion process. Pure oxygen, however, is very much better for substances that do not oxidize readily, because of the rapidity and completeness of combustion in its presence. With oxygen completion of the process is indicated when the outgoing stream from the absorption apparatus causes an ember on the end of a splinter of wood to glow brightly.

It may add to the understanding of the process to trace the air or oxygen stream through the whole apparatus (see fig. 11). It first bubbles through a strong solution of caustic potash, which removes most of the carbon dioxide; then passes through a large U-tube or drying-tower containing soda-lime or small pieces of NaOH, which removes the last traces of carbon dioxide; then through another U-tube containing calcium chloride, which removes moisture.¹ The dry gas passes into the combustion-tube; when it reaches the fine copper oxide it aids the oxidation of the organic substances, and carries along with it the carbon dioxide and steam produced, also any volatilized material which has not been oxidized, and brings them into contact with the coarse copper oxide, which completes the oxidation; thus the stream when it reaches the end of the tube consists of air or oxygen containing carbon dioxide and water-vapour. In passing through the calcium

¹ To insure thorough drying the air is sometimes finally bubbled through sulphuric acid. In this case H_2SO_4 must also be used as the absorbent in the place of the two calcium chloride tubes (Fig. 12).

chloride tube of the absorption apparatus the water is absorbed, and finally in bubbling through the caustic potash solution of the absorption bulbs the carbon dioxide is removed; the slight amount of moisture picked up here is removed by the straight calcium chloride tube (see fig. 12). The details of the method are given in the following experiment.

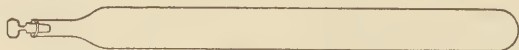


FIG. 13.

EXPERIMENT. *Combustion analysis of salicylic acid.* The combustion-tube has been charged and thoroughly heated as directed above. Remove the stopper at the end nearest the air-tank, quickly pour out the coarse oxide into a clean dry beaker, pull out the short spiral, finally pour out the fine oxide into another beaker and replace the stopper. Put the beakers and the spiral into a desiccator. Weigh accurately a weighing-bottle containing about 0.2 gm. of pure salicylic acid which has stood in a desiccator several days. Through a clean short-stemmed funnel pour the salicylic acid into the mixing-tube (see fig. 13); add some of the fine oxide carefully through the funnel in such a way that all the crystals of salicylic acid are carried along with the CuO into the mixing-tube. When the tube is half full, insert the stopper; hold the tube and stopper firmly and shake very vigorously. When well mixed, quickly empty the contents into the combustion-tube; rinse the mixing-tube by shaking successively with small portions of fine oxide until all the oxide has been transferred to the combustion-tube. Replace the spiral and

pour in the coarse oxide. Replace the stopper and connect with the air-purifying apparatus and start the air stream. The CaCl_2 tube remains at the other end of the tube. Reweigh the weighing-bottle.

Begin lighting the burners at the end near the calcium chloride tube. Start one burner at a time and with the lowest flame possible, then very gradually increase the flames in number and size. Do not heat the fine oxide at all. In the meantime weigh the calcium chloride absorption-tube and the caustic potash bulb with its calcium chloride tube (remove the plugs before weighing). When the coarse oxide has been brought to a dull red heat, the part of the tube which contains this having been covered with tiles, attach the absorption apparatus in place of the ordinary calcium chloride tube. Now start the heating of the other end of the tube, containing the fine oxide and the substance, very gradually, beginning at the far end. When the fine oxide is heated watch closely, and turn down the burners here if bubbles pass too rapidly through the potash bulbs. The bubbles should not go so fast that they cannot be easily counted. Finally, bring the whole tube to a dull red heat (never hotter). After thirty minutes (one hour if air is used) at this temperature begin to cool the tube by gradually turning down the burners from each end. Do not remove the tiles. Examine the end of the combustion tube for condensed water; if present vaporize it by careful heating at that point. If oxygen is used, change to an air-stream at this point so as to clear oxygen out of the absorption tubes before reweighing. During the first fifteen minutes of cooling pass the air stream more

rapidly to sweep out of the tube all water-vapour and carbon dioxide. Disconnect the absorption tubes, put on the plugs, and allow to cool in the balance room for one hour. When cool, reweigh after removing the plugs. Do not forget to attach the calcium chloride tube in the place of the absorption apparatus. Before the combustion-tube is used for another analysis it should be heated for an hour while dry air is passed through it. The KOH solution in the potash bulbs should not be used for more than two combustions.

The increase in weight of the U calcium chloride tube indicates the weight of the water produced by the combustion. One ninth of this is hydrogen, therefore the per cent of hydrogen present in the substance burned can be obtained by the following formula:

$$\text{Per cent H} = \frac{\text{wt. of H}_2\text{O produced} \times 100}{9 \times \text{wt. of substance burned}}.$$

The increase in weight of the potash bulb and straight calcium chloride tube is equal to the weight of the carbon dioxide produced. Carbon represents $\frac{3}{11}$ of this, therefore for calculating the per cent of carbon the formula used is:

$$\text{Per cent C} = \frac{\text{wt. of CO}_2 \text{ produced} \times 3 \times 100}{11 \times \text{wt. of substance burned}}.$$

The sum of the per cents of hydrogen and carbon deducted from 100 gives the per cent of oxygen.

If the substance contains *nitrogen*, oxides of nitrogen may be formed when the substance is oxidized as above. This necessitates a special modification of the

method, because these oxides are absorbed by caustic potash. A long copper spiral (12–15 cm.), which has been reduced to pure copper by dipping it while hot into alcohol,¹ is put into the end of the tube nearest the weighed absorption apparatus, in the place of part of the coarse oxide. When the nitrogen oxides come in contact with the hot reduced copper they are deprived of their oxygen by the copper, and nitrogen is set free.

Of course a free stream of air or oxygen cannot be used in this case until combustion is complete, otherwise the reduced copper spiral would become oxidized and be rendered useless. The air stream is used to clear carbon dioxide out of the tube at the start before the heat is applied to the reduced copper spiral; during combustion the air is shut off; when combustion is complete the air stream is again turned on to remove all the products from the tube.

To estimate the nitrogen alone in an organic substance the same tube as that described above for nitrogenous substances can be employed, provided a stream of dried carbon dioxide gas, instead of air, is used for removing the gases, etc., produced by the combustion and for clearing out the nitrogen and oxygen contained in the tube before the heating is begun. The absorption apparatus in this case is a gas burette (a burette closed with a glass cock at the top) having some mercury in the bottom to act as a valve, and filled with a 40% solution of caustic potash (see fig. 14). When bubbles no longer collect at the

¹ By this treatment any oxide adherent to the copper yields up its oxygen to oxidize the alcohol to aldehyde.

top of the burette and the latter remains full of caustic (i.e., when only carbon dioxide is passing out of the tube), the carbon dioxide is shut off and combustion is carried out by heating the tube gradually up to a red heat. When combustion is completed carbon dioxide is passed again until the tube is cleared of nitrogen, as shown by the volume of the gas in the burette remaining constant. The caustic potash absorbs all the products of combustion except nitrogen. The burette is allowed to stand for an hour to come to room temperature, the alkali being levelled up in the apparatus. The caustic potash in the reservoir is brought to exactly the same level as that in the burette, and the number

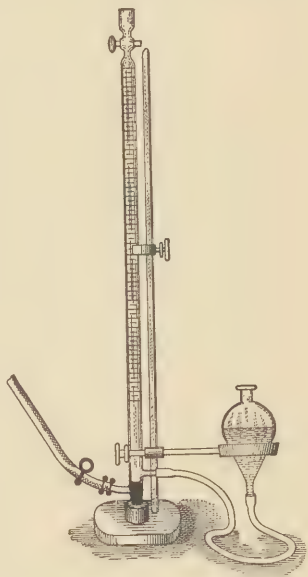


FIG. 14.

of cubic centimeters of gas is read off. The temperature of the nitrogen is found by placing a thermometer against the burette, with the bulb at the mid-level of the gas. The barometric reading (corrected for temperature) must also be taken. The results of the analysis are then computed by referring to specially prepared tables which give in grams the amount of nitrogen corresponding to 1 c.c. of the moist gas in the burette, at various temperatures and under various pressures (see Appendix, p. 405). In order to use

the table for nitrogen collected over alkali, add to the barometric pressure the difference between the vapour pressure of water and that of 40% potassium hydroxide at the temperature of observation (see table VI, p. 408).

An easier method of nitrogen estimation is the *Kjeldahl method*, by which the nitrogen in the organic substance is converted into ammonia by heating with pure sulphuric acid. The ammonium sulphate produced can then be treated with alkali, and the ammonia thus liberated distilled into a measured quantity of standard acid. From the amount of this latter which is thus neutralized, the amount of nitrogen contained in the organic substance can readily be calculated. Kjeldahl's method is extensively employed in biochemical analysis and will be found fully described in many of the laboratory manuals on that subject.

If halogens are present in the substance to be analyzed a silver spiral must be used in place of the reduced copper spiral. The silver combines with the halogens and prevents them passing into the absorption tubes, where they would be absorbed.

When sulphur is present lead chromate takes the place of the cupric oxide in the tube, lead sulphate being formed during combustion.

Having determined the percentage composition, a *provisional formula* for the compound may be found as follows: divide the percentage number of each element by its atomic weight, divide each of the resulting figures by the smallest of them (as the greatest common divisor ¹), and make use of these smaller figures, or the

¹ In many cases some other common divisor will have to be used.

nearest whole number, to express the number of atoms of each element in one molecule. An example will illustrate this. Alcohol was found by one analysis to contain 52.05% C, 13.13% H, and 34.82% O. Then

$$\text{C } 52.05 \div 12 = 4.337; \quad 4.337 \div 2.176 = 1.993$$

$$\text{H } 13.13 \div 1 = 13.130; \quad 13.130 \div 2.176 = 6.030$$

$$\text{O } 34.82 \div 16 = 2.176; \quad 2.176 \div 2.176 = 1.000$$

Therefore the formula may be $\text{C}_2\text{H}_6\text{O}$. The same percentage composition would, however, be shown by any substance having the formula $\text{C}_{2n}\text{H}_{6n}\text{O}_n$. It becomes necessary then to determine the number of atoms in the molecule by finding out the molecular weight; the value of n is thus discovered.

CHAPTER IV.

MOLECULAR WEIGHT DETERMINATION. THE NATURE OF SOLUTIONS. OSMOTIC PRESSURE. IONIZATION. COLLOIDAL SOLUTIONS. SURFACE TENSION. VISCOSITY.

IN order to understand fully the physico-chemical nature of solutions and the subject of molecular weight determinations it will be advisable briefly to review some of the cardinal points in physical chemistry which relate to these subjects. As we shall see later, gases and solutions in their physico-chemical behaviour are very much alike, so that a clear conception of the gas laws, which are well known and readily tested, will enable us to study more satisfactorily the nature of solutions.

The three important gas laws are as follows:

1. *Gay-Lussac's or Dalton's law*: provided its pressure remains unchanged, every gas expands by $\frac{1}{273}$ of its volume at 0° for each degree of rise of temperature.

Thus a gas occupying a volume of 1 litre at 0° will occupy 2 litres at 273° , if the pressure remains constant. In making calculations it should be remembered that the absolute temperature of 0° is 273° , and therefore for any temperature above 0° the absolute temperature is that temperature plus 273° . Another way of stating the law is that the volume of a gas (at constant pressure) varies directly with its absolute temperature.

2. *Boyle's law*: provided the temperature remains constant, the volume of a gas varies *inversely* as the pressure. Thus, if 1 litre of gas be compressed into the space of 0.5 litre, the pressure has been doubled.

3. *Avogadro's hypothesis*: under the same conditions of temperature and pressure, equal volumes of all gases contain the same number of molecules.

THE MOLECULAR WEIGHT OF GASES AND VAPOURS.

The relative weights of equal volumes of different gases, under the same conditions of temperature and pressure, must represent the relative weights of the molecules (Avogadro's hypothesis). If, then, we take the weight of one gas as the standard, the molecular weights of other gases can readily be ascertained. Hydrogen is the gas thus chosen, and since its molecule contains two atoms, we ascribe to it a molecular weight of 2. Similarly, oxygen has a molecular weight of 32, being sixteen times heavier than hydrogen. Two grams of hydrogen at 0° and 760 mm. Hg pressure has a volume of 22.4 litres. But 2 is the molecular weight of hydrogen; therefore if we take the number of grams of any other gas equivalent to its molecular weight this amount of gas will also occupy a volume of 22.4 litres (at 0° and 760 mm.). Such a weight in grams corresponding to the figures for the molecular weight is called a *gram-molecule* or a *mol*. In consequence of Boyle's law it must follow that if we compress a mol of any gas at 0° to the volume of 1 litre it will have a pressure of 22.4 atmospheres (i.e., 22.4×760 mm. Hg).

If, therefore, we know the volume, temperature, and pressure of a known weight of a gas it is easy by applying the above laws to determine its molecular weight. As an example, suppose that 0.2 gm. of a dry gas has a volume of 50 c.c. at 10° and 740 mm. Hg; what is the molecular weight?

$$50 \times \frac{273}{273 + 10} \times \frac{740}{760} = 46.899 = \text{c.c. at } 0^\circ \text{ and } 760 \text{ mm.}$$

But a mol occupies 22400 c.c. Then 0.2 gm. is $\frac{46.899}{22400}$ of a mol, therefore the mol is 95.4 gm. The molecular weight is 95.4.

Vapours obey the same laws as gases. Substances, solid or liquid, which can be vaporized by heat submit to a molecular weight determination as readily as gases. In practice the determination is made either by weighing a known volume of the substance in the form of vapour, or by measuring the volume of the vapour produced from a known weight of the substance.

A known volume of vapour is weighed when *Dumas' method* is used. By this method an indefinite quantity of the substance is vaporized in a flask-like bulb by heating the bulb in an oil-bath. The neck of this flask-like bulb is drawn out to a fine tip. When all the air is displaced from the bulb, and the substance is completely vaporized, the tip is sealed off in a flame. The temperature of the bath is recorded, also the barometric pressure. After cooling, the weight of the substance in the bulb and the capacity of the latter are accurately determined, and from these data the molecular weight

can be calculated. This method, while simple in principle, is nevertheless tedious in practice.

A much more useful method for general purposes is that of *Victor Meyer*, in which the volume of a known weight of vapour is ascertained by finding how much air is displaced in a closed apparatus when the substance changes to a vapour.

The apparatus,¹ as shown in the figure, consists of an elongated bulb continued above into a long neck closed at the top by a rubber stopper; from the neck passes a side tube which is connected by heavy rubber tubing with a gas burette. The bulb is suspended in a wide tube having a bulb-like expansion at its closed end (the upper two thirds of this tube should be wrapped with asbestos paper) and which contains some liquid with a boiling-point 40° – 50° above the vaporization temperature of the substance.

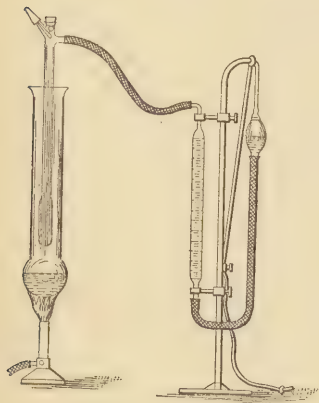


FIG. 15.

expansion at its closed end (the upper two thirds of this tube should be wrapped with asbestos paper) and which contains some liquid with a boiling-point 40° – 50° above the vaporization temperature of the substance.

EXPERIMENT. Fill the bulb of the outer tube two thirds full of distilled water; suspend the inner tube

¹ An excellent modification of this apparatus has been made by Bleier and Kohn, by which, instead of measuring air-displacement, the increase of pressure (the volume of gas in the apparatus being constant) due to the vaporization is measured by means of a mercury manometer. Before making an estimation the air-pressure in the apparatus is lowered by a suction-pump.

in it by means of a cork (this will have to be cut in two and then wired together again). By means of this cork also hang a thermometer in the steam-chamber and insert a bent glass tube as a steam-vent. Now boil the water (start the heating very gradually). When the thermometer registers a constant temperature, i.e., the boiling-point of the water,¹ connect the side tube with the gas burette and cork the inner tube tightly with a rubber stopper. Bring the water in the burette and in the reservoir to exactly the same level. If there is no variation from this level for 5–10 minutes the apparatus is ready for making an estimation. The entire column of air in the narrow tube has now come to the temperature of the steam surrounding it. Remove the stopper of the inner tube and place in position (supported by the glass rod which fits the extra branch tube and extends into the neck of the main tube, see fig. 15) a little sealed glass bulb containing a known weight of pure chloroform (the bulb having been weighed before and after filling). Fit the stopper tightly, and wait a few minutes to determine whether the volume of the air in the apparatus remains constant (as indicated by the level of the liquid in the burette). When constant, fill the burette exactly to the cock by raising the reservoir after having brought the burette into communication with the outer air by means of a two-way cock (either the cock of the burette or one specially inserted in the rubber tubing connection). Then close the cock, so that the burette communicates

¹ Boiling-point at 735 mm. barometric pressure is 99.1°, at 740 mm. 99.3°, at 745 mm. 99.4°, at 750 mm. 99.6°, at 755 mm. 99.8°, and at 760 mm. 100°.

only with the air of the system. Now drop the bulb to the bottom of the Victor Meyer tube by pulling the rod. Some glass wool has been put into the bottom of the tube to prevent injury. Vapor forms and hot air is pushed over into the burette. Level up the water in the burette with that in the reservoir. When the level remains absolutely constant for 10–15 minutes, close the cock of the burette. Measure the volume of the air displaced into the burette in exactly the same way as in nitrogen estimations (see p. 33), correcting for temperature, also for aqueous (see Appendix) and barometric pressure, and convert to the volume at 0° and 760 mm. (see p. 38). To make the calculation divide 22400 (22.4 L.) by the number of cubic centimetres of air displaced, and multiply this quotient by the weight of the chloroform vaporized; the product gives the weight of a gram-molecule of the substance, and the same figures express the molecular weight.

THE NATURE OF SOLUTIONS. OSMOTIC PRESSURE.

In their physical properties solutions are very different from gases. In attempting to apply gas laws to substances in solution it is evident that other methods than those used in the case of gases must be adopted to measure the pressure of the dissolved substance. We measure the pressure of a gas by means of a manometer, but it is obviously impossible to measure the pressure of a dissolved substance by the same means, for the only pressure which the manometer can record is that of the solution against the walls of its container. In the case of a gas the molecules are suspended in a vacuum; in the case of a solution they

are suspended in a solvent; the solvent of a solution is, therefore, analogous to the vacuum in which the gaseous molecules are suspended. For purposes of analogy is there any means by which the pressure of one gas suspended in another gas may be determined?

The metal palladium when heated to 200° allows hydrogen, but no other gas, to diffuse through it. If, therefore, a small vessel of heated palladium containing nitrogen be suspended in a confined atmosphere of

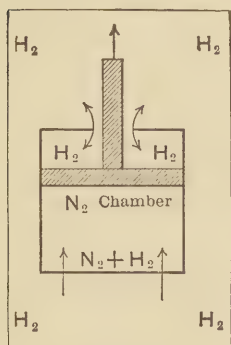


FIG. 16.

hydrogen, the latter being kept under constant pressure, hydrogen will diffuse into the vessel but no nitrogen will diffuse out. In consequence of this the pressure inside the palladium vessel will become greater than that outside, and the difference between the two at the end of the experiment will represent the pressure of the nitrogen. The figure shows a piston working freely in the palladium box; hydrogen passing into the nitrogen chamber (indicated by arrows) increases the pressure on the under surface of the piston so that the latter moves upward.

This gives us an indication of how it may be possible to measure the pressure of a dissolved substance, for in the above experiment we can conceive of the nitrogen as being in solution in hydrogen; indeed, to make the case still plainer, we can start the above experiment with a mixture of hydrogen and nitrogen inside the palladium vessel and measure increase of pressure. The hydrogen

really dissolves in the palladium membrane, and is given off on the other side where the partial pressure of hydrogen is low.

This experiment shows us that if we could but obtain a membrane allowing only one of the constituents of a solution (i.e., the solvent) to pass through it, then we could measure the pressure which the other constituent (i.e., the solute) exercises. An example of such a membrane is a film of copper ferrocyanide. Since this film of copper ferrocyanide is too fragile to exist unsupported, it may be deposited in the pores of a porous cell (such as is used for electric batteries), and the following method may be used in preparing it.

A fine-grained porous cell, about four inches long and one inch inside diameter, is closed with a perforated rubber stopper, through which passes a glass tube connecting with a suction-pump. The cell is placed in water, and the water is sucked through the pores; then in acid, then in water again. By this means the pores of the cell are thoroughly cleaned. When clean, the cell is placed in a 15 per cent solution of potassium ferrocyanide, and suction is maintained until the pores are completely filled. The inside and the outside of the cell are then thoroughly washed with distilled water, after which it is immersed for several hours in a 25 per cent solution of copper sulphate. The copper sulphate reacts with the potassium ferrocyanide in the pores of the porous pot, so that a fine precipitate of copper ferrocyanide is deposited. After washing in water the cell is ready for use.

If a solution of cane sugar be placed inside such a cell and this be suspended in water, the latter will pass

into the cell and cause the volume of fluid in this to increase, so that, if a vertical glass tube be connected with the cell, fluid will mount up in it to a very considerable height; or if we connect a pressure-gauge (manometer) with the cell, we shall be able to measure the pressure instead of the increase of volume. If a gram-molecular¹ (more accurately, *weight normal*) solution of cane sugar be employed, the pressure in the cell as recorded by the mercury manometer comes to be equal to that of 22.4 atmospheres. This pressure, however, can seldom be attained, for it is too great for the fine film of copper ferrocyanide to withstand.² The film of copper ferrocyanide ruptures, and an escape of the fluid takes place. The pressure thus demonstrated is called *osmotic pressure*, and a membrane of the nature described is called a *semi-permeable membrane*.³ None of the membranes used for this purpose are perfect semi-permeable membranes, for traces of solute can pass through them.

Some membranes, such as porous plates the spaces of which have been *partially* blocked by fine non-gelatinous precipitates so that the capillary pores are about 0.5μ .

¹ By gram-molecular solution is meant the molecular weight of a substance in grams dissolved in an amount of solvent sufficient to make 1 L. of solution (Arrhenius), while by weight normal is meant a solution in which the gram-molecular weight of substance is dissolved in 1000 gm. of solvent.

² An actual pressure equal to 22.4 atmospheres has recently been observed by Morse and Frazer by using a specially constructed apparatus.

³ Solutions of salts and other substances which become dissociated in solution do not behave according to this law (see p.57).

in diameter, have a sieve-like action in developing osmotic pressure, holding back the larger molecules and letting water pass through. In some other cases there is involved the question of solubility of a substance in a membrane (cf. palladium experiment), for instance if a membrane well soaked with water be interposed between moist ether and a mixture of benzene and ether, ether will dissolve in the membrane and pass over into the benzene, but benzene will not pass through into the ether.

It has been found that the osmotic pressure of all gram-molecular solutions corresponds to a pressure of 22.4 atmospheres, which, it will be remembered, is the pressure of a gram-molecule of gas compressed to the volume of a litre. Knowing this, we can calculate what the pressure of any dissolved substance in solution will be. Thus, the pressure x of a 1 per cent solution of cane sugar may be calculated from the proportion: Molecular solution : 22.4 atmospheres :: 1% solution : x . Solutions which obey the laws of osmotic pressure most accurately are those of the strength of decinormal solutions.

These facts show us that the osmotic pressure of a solution must be analogous to the pressure of a gas; the volume in both cases being easily measured, we are therefore in a position to test the gas laws in solutions.

1. According to Gay-Lussac's law, the osmotic pressure should be proportional to the absolute temperature. That this is so is proved by the following observation. A 1 per cent solution of cane sugar at 14.2° has an osmotic pressure of 510 mm. Hg, and at 32° of 544 mm.

Hg. According to calculation it should be 540.6 mm. Hg (practically agreeing with the finding), thus

$$510 \times \frac{273+32}{273+14.2} = 540.6.$$

2. According to Boyle's law, the osmotic pressure should be directly proportional to the concentration of the solution—or, in other words, inversely proportional to the volume of the solution. By comparing the osmotic pressures of cane sugar solutions of varying strengths (at the same temperature), the following values have been obtained:

Gram-molecules in 1000 gm. Water.	Osmotic Pressure in Atmospheres.
0.1	2.35
0.2	4.70
0.6	14.09
1.0	23.49

It will be seen that the law applies.

3. According to Avogadro's hypothesis, all equimolecular solutions (i.e., solutions in which the weights of the solutes in a given quantity of solution bear the same ratio to one another as the molecular weights of those substances) ought to have the same osmotic pressure. As already stated, this has been found to be the case.

Theoretically, the measurement of the osmotic pressure would be a simple enough way of determining the molecular weight, but, in practice, the method cannot be used, because, unless elaborate precautions be taken, any considerable pressure in the cell mechanically ruptures the membrane, and so allows the fluid to leak and the pressure to fall. The method is of interest mainly because it shows us the striking analogy between a gas and a solution. It shows us that the osmotic pressure is virtually the same as the gaseous pressure which any substance would exert were it present as a gas in the same volume as that occupied by the pure solvent: that if the solvent were suddenly removed the dissolved molecules might be considered as remaining suspended as a gas and the gas would be under a pressure corresponding to its volume.

Considerable discussion and criticism of the present views as to the nature of osmotic pressure has recently been brought forward.

Biological Methods for Measuring Osmotic Pressure. If, in the above experiment with cane sugar solution, instead of placing the cell in water we had placed it in a solution of cane sugar weaker than that contained in the cell, then the osmotic pressure would not be so great as in the previous case, because water would pass into the cell only until the strength of the solution came to be the same as that outside it. This fact leads us to an important conclusion, viz.: that the relative strengths of two solutions can be ascertained by seeing whether osmosis occurs between them when they are separated from one another by a semi-permeable membrane.¹

¹ This is true only for solutions of diffusible substances in the same solvent (water).

In the case of the copper ferrocyanide cell, above described, we could determine this fact by measuring the pressure inside the cell. If, however, we employ a closed sac of some semi-permeable membrane filled with one of the fluids, then we could, by suspending this sac in some other fluid, tell if osmosis had occurred, by seeing whether the sac became distended or the reverse. In the case of the red blood-corpuscles we have a structure analogous to this. The envelope of the corpuscles acts like a semi-permeable membrane; it allows water to diffuse through it, but not salts.¹

Now a corpuscle contains a solution of salts and hæmoglobin, and if it be placed in a fluid containing in solution the same number of molecules as is contained in the fluid inside the corpuscle, then no osmosis will occur in either direction and the corpuscle will remain unchanged in volume. Such a fluid which is iso-osmotic with the fluid inside the corpuscle is called an *isotonic* solution. If the corpuscle be placed in a solution which is weaker than that contained in the corpuscle, then water will diffuse in and the corpuscle will distend and may ultimately burst. Such a solution is said to be *hypotonic*. If the corpuscle be placed in a solution which is stronger than that of its fluid contents, then water will diffuse out of the corpuscle, so that the corpuscle will shrink. Such a solution is called *hypertonic*.

This change in the volume of the corpuscle may be observed under the microscope, and a quantitative expression also of the change in volume of the corpuscle may be obtained by using an instrument called a hæmatocrit. This consists of a graduated narrow capillary tube, about seven centimetres long. At one end the tube is widened so as to give space in which the fluids may be mixed. Blood is drawn into the capillary by means of a syringe and its volume accurately measured. The pipette is then closed at each end by small, accurately fitting, metal plates held in position by a spring.

¹ The corpuscles are, however, permeable for alcohols, free acids, and alkalies, ammonium salts and urea.

The tube is then placed horizontally in a rapid centrifuge and rotated so that the corpuscles are thrown to the outer end. The graduation mark at which the column of corpuscles stands is then noted.

In another tube a drop of the same blood is mixed with an equal volume of the fluid whose molecular concentration it is desired to determine. The exact amount of blood and fluid taken is read off from the graduations of the tube. The two fluids are then sucked into the wide part of the tube and mixed by means of a fine platinum wire. The tube is then closed and centrifuged. If the corpuscles stand at the same level as for blood alone, then we know that the solution is isotonic with the blood-corpuscles, which means that they must also be isotonic with the plasma. If the column of corpuscles be longer, then we know that their volume must have been increased, and that the fluid under examination is hypotonic. If the column of corpuscles be shorter, the solution is hypertonic.

Iso-osmotic solutions are isotonic to the same cells. Solutions of corresponding concentration (as, one-tenth gram-molecular) of most organic compounds (except metallic salts, acids and bases) are iso-osmotic; solutions of ionizable substances (p. 57) have a greater osmotic pressure than solutions of other substances; a comparison is made in the following:

Cane sugar	1.00
Potassium nitrate	1.67
Sodium chloride	1.69
Calcium chloride	2.40

These figures are the *isotonic* coefficients of the substances.

In the case of living cells it seems to be necessary to take into account selective permeability, for example, the tadpole when immersed in a hypertonic sucrose solution (as 8%) shrinks noticeably in twenty-four hours, there being no injury to the epithelium; on the other hand a tadpole placed in hypotonic sucrose solution (3%) does not swell up, the epithelial cells are not noticeably permeable to water passing in.

EXPERIMENTS. (1) *Osmotic Pressure Effects in a Vegetable Membrane.* Shave very thin slices from a red beet, mount some on a slide with very little water, and examine microscopically. Now drop a few crystals of NaCl on the slice and observe that the red substance shrinks, the hypertonic solution having caused *plasmolysis*.

(2) *Osmotic Pressure Shown by an Animal Membrane.* Float an egg in 20% NaCl, the uppermost end contains an air space, open the shell at this point, removing it down to where the egg membrane joins the shell. Stretch a number of strips of parchment paper over the membrane and on to the shell, cementing them to the shell; shellac the cemented ends. The parchment gives support to the membrane. To the opposite end of the egg attach a small upright glass tube by applying melted paraffin, run a long needle down the tube and carefully drill a hole through the shell and egg membrane. Immerse the egg in distilled water. After standing some time the egg contents will have swollen sufficiently to force egg white up into the tube.

(3) *Osmotic Pressure Shown by an Inorganic Membrane.* (a) Select a long narrow crystal of CuSO_4 ,

tie a thread about the middle, fasten the thread to a glass rod lying across the top of a beaker so that the crystal hangs in potassium ferrocyanide solution. A copper ferrocyanide membrane forms, which becomes distended by the passage of water through it toward the copper sulphate.

(b) Fill the bent portion of a U-tube with melted agar solution, cool, when solidified fill one limb with CuSO_4 solution, the other with potassium ferrocyanide solution. On standing several days a sharply definite area of copper ferrocyanide forms midway in the agar.

(c) Drop a small lump of CaCl_2 into some saturated potassium carbonate solution. On standing a membrane develops and *grows*, making plant-like forms.

MOLECULAR WEIGHT OF SUBSTANCES IN SOLUTION.

Is there then no easily measurable physical property of solutions which depends on their molecular concentration, and which will, therefore, bear a relationship to the osmotic pressure? The vapor pressure of a solution is proportional to its osmotic pressure, but the method of determining vapor pressure is a difficult one to carry out. It has been found that the temperature at which a solvent freezes is lowered when a substance is dissolved in it, and that the amount of this lowering, or *depression of freezing-point*¹, is for dilute

¹ *Cryoscopy* is a name given to freezing-point determination.

An interesting explanation of the fact that C is quite different for different solvents is furnished in Raoult's extension of his

solutions proportional, not, in general, to the chemical nature of the substance, but to the number of molecules of substance dissolved in a given volume. (The same holds true for the elevation of boiling-point, which can be most easily demonstrated with the McCoy apparatus. This method, however, will not be described here.) This being so, it follows that all gram-molecular solutions in the same solvent must lower the freezing-point to an equal extent. The depression of freezing-point produced by a gram-molecular quantity of a substance dissolved in 1000 gm. of the solvent (weight normal solution) varies for different solvents:

	Depression of Freezing-point,
For water	1.86°
“ benzol	5.00°
“ phenol	7.20°
“ acetic acid	3.90°

These figures are called the constants (or *C*) of the solvents. They correspond, therefore, to an osmotic pressure of 22.4 atmospheres.

The apparatus in which the freezing-point determinations are made is known as Beckmann's. This consists of a large test-tube, to contain the substance, suspended

law: if a gram-molecule of a compound be dissolved in 100 gram-molecules of solvent (except water), the freezing-point of the latter will be depressed by about 0.62°.

in a somewhat larger test-tube, so as to form an air-jacket between the two tubes. The outer test-tube is placed in a freezing-mixture of iced water and salt contained in an earthenware jar (which has been wrapped round with flannel to diminish the heat-conduction). The freezing-mixture is stirred with a loop of wire as represented in the diagram. In the inner test-tube is suspended the bulb of a Beckmann thermometer. This thermometer does not give absolute readings of temperature as does an ordinary thermometer. It is used only for demonstrating the difference in temperature at which two solutions freeze, or with certain modifications it may be used to tell the different temperatures at which two solutions boil. Before using the thermometer for freezing-point demonstrations the meniscus of the mercury column must be adjusted so that it stands within the scale (high up) at the temperature at which the solvent used freezes or crystallizes. To make this adjustment the bulb of the thermometer is placed in iced water, and if it be found that there is too much mercury to bring the meniscus within the scale, then the upper end of the thermometer is tapped with the fingers so as to cause the mercury at the top of the reservoir, which is connected with the upper end

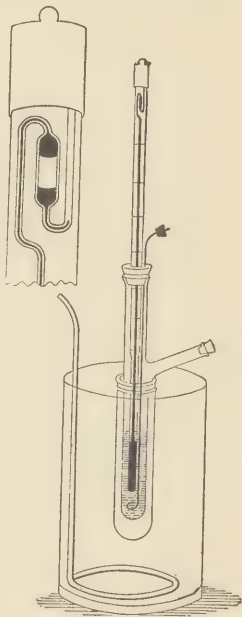


FIG. 17.

of the thermometer tube, to fall to the bottom and so to become disconnected from the mercury column in the thermometer tube. Should the meniscus of mercury stand below the scale at the freezing-point of water, or of the other solvent used, then the thermometer must be inverted, and, by tapping, more mercury can be added to that in the tube.

For making the actual freezing-point determination the inner tube of the apparatus is partly filled with the solution under examination so that the latter comes a little above the bulb of the thermometer (see fig. 17). The tube is then placed directly in the freezing-mixture until the mercury, having fallen to its lowest level, begins to rise again, after which the tube is removed from the freezing-mixture and placed in the larger test-tube, as before described. The cooling is then proceeded with until the meniscus of mercury stands at a constant level. During cooling, the fluid is kept constantly in motion by means of a platinum wire, bent into a loop as shown in the diagram. The reading is taken whenever constant and compared with the reading obtained when pure water (or whatever other solvent is used) is frozen. This difference is designated by Δ .¹

¹ Care should be taken that the supercooling is not excessive. If this be so, a correction is necessary because the formation of ice (pure water) lessens the volume of the solution, therefore, the depression is greater than it would be if only a trace of ice is present. For aqueous solutions 1.25% of Δ is added to the observed thermometer reading for each degree centigrade of supercooling, and by deducting from the freezing-point of water the true Δ is obtained. For example, suppose the freezing-point of water was at 4° , that of the solution at 2° , and the point of supercooling at 0° . Δ is 2, then $2 \times .0125 = .025$; $2^{\circ} + .025 = 2.025^{\circ}$; $4^{\circ} - 2.025 = 1.975^{\circ} = \text{corrected } \Delta$.

Since this constancy of C , for any given solvent, is the point on which the method depends, the following experiment should be performed to demonstrate that for water C has the value given to it above.

EXPERIMENT. Weigh out a quantity of pure dry urea corresponding to one-tenth its molecular weight in grams (i.e., 6 gm.); dissolve this in 100 gm. of distilled water. Compare the freezing-point of this solution, corrected for supercooling, with that of pure water. It will be found to freeze almost exactly at 1.86° lower than that of water.

In determining the molecular weight of any substance we must first of all choose the most suitable solvent for it, and, in an accurately weighed quantity of this, dissolve an accurately weighed quantity of the substance under examination. Knowing what C for our solvent is,—in other words, through how many degrees centigrade the freezing-point of our solution would be lowered were a gram-molecular quantity per 1000 gm. of solvent taken,—if we find the freezing-point actually lowered to a less extent than this, we know that less than a gram-molecule must have been dissolved, the actual amount less than this being proportional to the difference from C recorded by the thermometer. In other words, the depression observed, represented by Δ , is to C as the strength of the solution used $\left(\frac{\text{weight of substance}}{\text{weight of solvent}} \right)$ is to that of a gram-molecular solution (or rather a solution containing a gram-molecule dissolved in 1000 gm. of solvent, see foot-note, p. 44).

$m = \frac{S}{L} \times \frac{C}{\Delta}$, where S equals the weight of substance used in grams; L , the weight of solvent in grams. $\frac{S}{L}$, when solved, gives a decimal fraction expressing what part of 1 gm. of the substance is dissolved in 1 gm. of solvent; therefore, to calculate the gram-molecule (the amount dissolved in 1000 gm. of solvent), m must be multiplied by 1000, and M equals the *molecular weight* in the equation $M = \frac{S}{L} \times \frac{C}{\Delta} \times 1000$. For example, let us take a determination on a one per cent cane-sugar solution, the Δ is about 0.054° . The molecular weight of the sugar, therefore, is, $\frac{1}{100} \times \frac{1.86}{.054} \times 1000 = 344$. According to the formula, $C_{12}H_{22}O_{11}$, it should be 342.

The Δ of blood and of urine are sometimes determined. That of human blood is about 0.55° . In case of drowning the blood is diluted, therefore the Δ is much less; if a person were killed before being thrown into the water the Δ would not be lessened.

IONIZATION.

The method is not, however, applicable to all substances, even though they be readily soluble in the above-mentioned solvents. This is on account of the fact that in the case of those the extent to which a gram-molecular quantity per 1000 gm. of solvent lowers the freezing-point is greater than C . Practically all metallic salts and most acids and bases when in aqueous solution are included in this category. To demonstrate this let us determine the depression of freezing-point produced by a gram-molecular solution of sodium chloride.

EXPERIMENT. Weigh out one-tenth (one-twentieth is better) the molecular weight of pure sodium chloride in grams and dissolve, as in the case of urea, in 100 c.c. of pure distilled water. Determine the depression of the freezing-point in Beckmann's apparatus. It will be found to be considerably greater than 1.86 (viz., about 3.35).

Knowing that 1.86 is Δ for a gram-molecular solution, it is easy to calculate how many gram-molecules per litre (X) a Δ of 3.35 will represent, thus:

$$1.86 : 1 :: 3.35 : X; X = 1.8.$$

To ascertain the actual osmotic pressure of the sodium chloride solution we must accordingly multiply 22.4 atmospheres by 1.8. This gives us about 40 atmospheres.

What then is the cause of this deviation from the law? The answer to the question is furnished by comparing the *electrical conductivity* of the two classes of solutions. Solutions of those substances which obey the above law will be found to be bad conductors of electricity—*non-electrolytes*,—whereas solutions of those substances which do not obey it will be found to be good conductors—*electrolytes*. This discovery, viz., that solutions which conduct electricity appear, from the determination of Δ , to have a greater number of molecules than those which do not conduct, has led chemists to the conclusion that certain of the molecules in such solutions must split up into smaller parts, called *ions*, and that it is only when this *dissociation* of molecules into ions takes place that it is possible for the solution to conduct electricity. In fact, our whole

conception of the conduction of electricity in solutions is based on this hypothesis. It is supposed that every molecule of substance is charged with positive and negative electricity, which in the intact molecules so neutralize one another that we do not appreciate either. When these molecules are suspended in solution, however, they show a greater or less tendency to split up into ions, one set of which carries positive electricity and the other negative electricity. These ions wander about the solution much as if they were independent molecules.

When an electrical current is passed through a solution which has undergone dissociation into ions, the ions tend to collect at the two poles and yield up their electrical charges. Those which collect around the positive element or anode are called *anions*, and those collecting around the negative element or cathode are called *cations*. Anions are charged with negative electricity, and cations with positive electricity. Examples of anions are oxygen and the acid portion of salts, for example SO_4 , Cl , etc.; the cations include hydrogen and metals.

EXPERIMENT. Put some strong NaCl solution in a beaker, add a few drops of phenolphthalein solution, and immerse in the liquid a pair of battery plates, consisting of a strip of sheet zinc and one of copper soldered together at one end and separated in the liquid. As the electric current passes, sodium ions travel to the copper plate and give up their electric charges, becoming metallic sodium, which attacks the water and forms NaOH in the region of the copper plate, therefore a pink zone (OH ions) appears at this point.

When solutions of acids undergo ionization, the cation H is that which confers the acidic properties to the solution. An un-ionized acid does not act like an acid; for example, H_2SO_4 dissolved in toluene does not ionize and will not give off hydrogen in the presence of zinc. (Also see experiment under Picric Acid, p. 307.) On the other hand, hydrogen itself, as the gas or in solution, shows no acid properties. We must assume, therefore, that the hydrogen ion is something different from the hydrogen atom. The same is true for other ions: they are not the same as the free elements or groups of elements; they are particles with opposite electrical charges which behave like molecules.

It is usual to designate the various ions by their symbols, affixed to which is the sign $\cdot$ for cations (e.g., $\text{H}\cdot$, $\text{Na}\cdot$, etc.) and $'$ for anions (e.g., Cl' , NO_3' , etc.). Some ions must carry two or more units of electrical charge, however, for otherwise in the case of such a substance as H_2SO_4 there would be an excess of positive electricity in the molecule. The ion SO_4 must therefore carry two charges of negative electricity and be represented by the sign SO_4'' . The valence of the ion usually agrees with the number of unit charges of electricity which it carries.

The coefficient of dissociation therefore indicates what proportion of the molecules have become split up into ions. For molecules which can yield only two ions it cannot be greater than 2, but for those splitting into more than two ions it may exceed this number. In the concentration of a 1 per cent solution it is 1.82 for KCl , 1.67 for KNO_3 , 2.11 for K_2SO_4 , 2.18 for Na_2CO_3 , and so on.

The amount of dissociation that a salt or acid undergoes in solution depends very largely upon the dilution: the greater the dilution, the greater the dissociation, and therefore the higher the coefficient.¹ For example, the coefficient of a 0.27 per cent solution of sodium chloride is 2, as against 1.9 for a 1 per cent solution.

In a solution of an electrolyte there is a condition of equilibrium between molecules and ions. The molecules are continually dissociating and simultaneously ions are uniting to form molecules. Reactions between electrolytes proceed rapidly, because as fast as ions are used up more molecules ionize in the effort to restore equilibrium. Most organic compounds react slowly because of absence of ions.

EXPERIMENT. To two test-tubes add a few c.c. AgNO_3 , to one add NaBr , to the other $\text{C}_2\text{H}_5\text{Br}$.

Occasionally, when a substance is dissolved, instead of dissociation there occurs a fusion of several of the molecules. In such a case the freezing-point or boiling-point method would give too high a molecular weight. This tendency to form complex molecules most frequently manifests itself with organic substances containing hydroxyl or cyanogen groups, and when chloroform or benzol is the solvent.

Many liquids polymerize, that is, their molecules *associate*. The condition of water is supposed to be represented by $(\text{H}_2\text{O})_4$. Liquid hydrocyanic acid is $(\text{HCN})_6$. Next in order of association are formic acid

¹ For example, a solution of 0.073 gm. HCl per litre $\left(\frac{N}{500}\right)$ is completely dissociated.

and methyl alcohol. The greater the polymerization of the solvent, the greater will be the dissociation of an electrolyte.

EXPERIMENT. Add a few drops of phenolphthalein solution to 25 c.c. of neutral ethyl alcohol, then one drop of concentrated NH_4OH , no colour change; dilute with water, and a pink colour develops because ionization of the hydroxide takes place in the dilute alcohol.

COLLOIDS.

Substances may be distributed or dispersed in a liquid in various ways. Insoluble substances in the form of a coarse powder when shaken with a liquid are momentarily suspended in the liquid but quickly settle out, while very fine powders may remain suspended a considerable time. As the size of the particles is decreased, the time that they remain in suspension is increased, until a stage is reached at which the particles do not settle. Mercuric sulphide may be prepared by passing hydrogen sulphide into a neutral solution of mercuric chloride; no precipitation occurs; to the eye it seems a perfectly uniform solution. Under the microscope, however, the liquid is seen to be full of small particles in active motion (Brownian). Such an apparent solution is classed not as a suspension but as a *SUSPENSOID*. In the case of most suspensoids, the particles are too small to be seen with the microscope.

Not only may solid particles be suspended in a liquid, but liquids also may be suspended in liquids as minute droplets. For example, if an oil be shaken very vigorously with water, the oil is broken up into drops

which remain suspended for a moment. If the oil be treated with an emulsifying agent and then mixed with water, the oil is present as microscopically fine drops, each drop being covered with a film of the emulsifying material. Such an *emulsion* remains apparently homogeneous for some time.

There are certain complex organic substances which in solution are believed to be present in the liquid phase as film-covered droplets, which are infinitely smaller than emulsion drops. Such substances are called **EMULSOIDS**. Thus emulsoids differ from suspensoids in that the former are in the liquid phase.

Other substances dissolve, forming what we call true solutions, which we conceive to be liquids having molecules of the solute uniformly distributed throughout the solvent. However, it has been shown in the case of some solutions that the centrifuge can cause them to become non-homogeneous, the solution becoming more concentrated at the bottom of the tube. It would, therefore, be better to call such solutions *molecular disperse solutions*. The finest particles of suspensoids and emulsoids are not separate molecules, but agglomerations of molecules.

Thus there is a regular gradation in dispersion mixtures from molecular dispersoids to emulsoids and suspensoids and then to emulsions and suspensions. The diameter of the particles is said to be as follows:

Molecular dispersoids: $0.1\text{--}1.0\mu\mu$.¹

Emulsoids	}	$1.0\mu\mu\text{--}0.1\mu$.
Suspensoids		

Suspensions and emulsions: greater than 0.1μ .

¹ A $\mu\mu$ is one millionth part of a millimeter. A μ is one thousandth part of a millimeter.

As a rule suspensoid particles are much larger than emulsoid particles, in the case of colloidal gold, however, some particles as small as $3-10\mu\mu$ have been obtained.

Emulsoids and suspensoids are classed together as colloids.

An approximate idea of the size of the particles can be obtained by graded filters, the size of their pores being known. By this method colloidal Prussian blue is shown to have the largest particles and dextrin the smallest.

The following list gives in order some of the substances having particles intermediate in size:

Prussian blue.

Colloidal ferric hydroxide.

Casein (in milk).

1 per cent gelatin.

1 per cent hæmoglobin.

Serum albumin.

Albumoses.

Dextrin.

The rate of diffusion of colloidal substances is very slow compared with that of non-colloidal substances; for instance, it takes egg albumin 21 times as long as it does sodium chloride to diffuse to the same extent, and caramel 42 times as long. Colloids will not diffuse through a gelatinous partition such as an animal membrane or parchment paper, whereas crystalloids readily diffuse (diffusion through a membrane is called osmose¹). Therefore colloids and crystalloids can be separated

¹ Do not confuse osmose with osmotic pressure phenomena.

from one another by dialysis (see p. 19). Some colloidal solutions have been shown to exert osmotic pressure. A 1% hæmoglobin solution gave 3.5–4.35 mm. (Hg) pressure, while a 10% gelatin solution at 23° gave 70 mm. pressure which was remarkably constant for a long time. In these experiments a dialyzing membrane was the osmotic membrane, so that the effect of diffusible impurities was eliminated. Apparently the colloidal particle exerts the same effect in causing osmotic pressure as a molecule of a crystalloid. The number of molecules aggregated together into a colloidal agglomerate is variable and may be different at different times in the same solution. Whenever the colloidal clumps become larger the osmotic pressure is lessened.

Because of this variability it is obviously impossible to determine molecular weight by the usual methods. Depression of freezing-point is valueless for the purpose, even aside from the question of variable aggregation, because a solution which has an osmotic pressure of 50 mm. gives only 0.005° depression of freezing-point.

Evidence of the presence of colloidal clumps in a solution can be obtained with the aid of the ultra-microscope. A powerful beam of light is passed into the solution, the axis of the microscope being at right angles to the ray. The particles divert or reflect the light. This is on the same principle as the Tyndall phenomenon observed in the scattering of light by dust particles in the air when a sunbeam passes into a room.

What is seen in the colloidal solution by means of the microscope are bright moving specks on a dim background or else a haze of light.

In the case of suspensoids the size of the clumps can be estimated by means of this apparatus. One specimen of colloidal gold solution has been prepared having particles too small to be distinguished. Solutions of emulsoids which have been dialyzed until electrolytes have been removed probably have particles less than $20\mu\mu$ in diameter; they cannot be distinguished. These show the haze of light. Extreme dilution is necessary to cause sufficient separation of the clumps of any colloidal solution from one another to make them distinguishable.

In the presence of electrolytes, particularly salts, colloids aggregate into larger clumps; under these circumstances even emulsoid particles can be detected. Thus the digestion of protein by pepsin, it is said, can be watched with the ultra-microscope (HCl present).

Colloidal solutions can be prepared that are optically negative to the ultra-microscope, while, on the other hand, solutions of some crystalloids, as sucrose, cannot be obtained which are optically negative. Apparently, it is safest to consider all solutions as being ultimately non-homogenous.

It is probable that the motion of colloidal particles is due to the same force as causes the movement of molecules and of ions. This motion and also the bumping of the colloidal particles by the rapidly moving ions greatly favor the agglutination of the particles to form larger masses.

Lintner's soluble starch in 0.01% solution gives a faint diffuse polarized light-cone. A 0.01% gelatin solution shows tiny whitish particles, barely visible, and freely moving; if the solution is prepared by boiling, individual particles cannot be seen, but only a light-

cone. A 0.07% solution of specially purified glycogen showed numerous extremely small white particles (in motion). If various proportions of alcohol are present in different portions of a glycogen solution, the particles become easily observable, the size of the clumps increasing steadily with increase in alcohol concentration.

Solutions of suspensoids do not gelatinize, are not viscid, and are coagulated by a small quantity of electrolytes. They are irreversible colloids, that is, after being precipitated they cannot be put into colloidal solution again.

EXPERIMENT. Prepare colloidal Prussian blue as follows: measure into one test-tube 10 c.c. N/50 ferric chloride, into another 10 c.c. N/50 potassium ferrocyanide, pour the two solutions simultaneously at the same rate into a clean beaker. A blue solution free of precipitate is secured. Shake some of the solution in a test-tube; it does not form a foam, no viscosity. Dilute about 5 c.c. with 25 c.c. of distilled water; there is no precipitate. To 5 c.c. of the diluted solution add 5 c.c. of magnesium chloride solution. On standing a blue precipitate forms. Save the more concentrated Prussian blue solution for a later experiment.

Even suspensions of some fine powders, as lamp-black or kaolin, are precipitated by electrolytes in a similar manner to suspensoids. The power of electrolytes to precipitate suspensoids is proportional to the electrical conductivity of the electrolyte in the solution. A 0.7 gram-molecular solution of acetic acid and a 0.0038 gram-molecular solution of hydrochloric acid have the same precipitating power toward

colloidal arsenious sulphide, and have practically the same conductivity (therefore the same H ion concentration).

Some colloids are electro-positive while others are electro-negative; that is, when an electrical current is passed through the solution the particles travel to the cathode or to the anode respectively. Suspensoids are precipitated by ions of opposite electrical sign; electropositive colloids, as ferric hydroxide, are precipitated by anions, as Cl , SO_4 , while electronegative colloids, as arsenious sulphide, are precipitated by cations, as H , K , Mg . The colloidal particles attract ions carrying an opposite electrical charge; their electrical charge is thus neutralized. In consequence the surface tension between the particles and the water becomes greater. This leads to agglomeration of the colloidal clumps, progressing steadily until the masses are large enough to separate out as a precipitate. Suspensoids of opposite electrical sign will mutually precipitate one another, as illustrated by the experiment.

EXPERIMENT. To 5 c.c. of colloidal arsenious sulphide solution add gradually colloidal ferric hydroxide solution, while shaking, until a precipitate forms.

Emulsoid solutions are viscid, they tend to gelatinize, and are not coagulated by small amounts of electrolytes. They are *reversible*, that is, after being precipitated by strong solutions of salts or by alcohol, etc., the precipitate can be redissolved in water.

EXPERIMENT. Reversible colloids. Pour about 5 c.c. of warm 5% gelatin solution into a test-tube. Shake

well; the froth indicates viscosity. Cool the tube with running tap water; the solution becomes a jelly. Warm again until fluid, add an equal volume of magnesium chloride solution; no precipitation occurs.

An *aqueous* colloidal solution in the liquid state is called a *hydrosol*, in the gelatinized state a *hydrogel*.

Suspensoids cannot travel into an emulsoid solution when the latter is in the gel state, while crystalloids readily diffuse into the gel.

EXPERIMENT. Take two test-tubes containing 1% agar-agar solution in the gel state. Into one pour Prussian blue solution, into the other pour some ammoniacal copper hydroxide solution (to 5 c.c. concentrated copper sulphate solution add ammonia water until the precipitate is just redissolved). Let the tubes stand an hour or more; the Cu solution penetrates the agar, while the colloidal suspension does not. At the end of the session empty the tubes, leaving the agar in, rinse out, note the condition of the agar.

Some emulsoids are not colloidal when dissolved in a solvent other than water; for example, tannic acid dissolved in glacial acetic acid is a molecular dispersoid, but in water it is a colloid. Emulsoids require a high concentration of salts to effect precipitation from a solution. This action is not an ion effect concerned with electrical charges as in the case of suspensoids, but is a salting-out process. Specially purified serum protein was found to be neither electropositive nor electronegative, yet it was precipitated by salts from neutral solution.

When an emulsoid is added to a suspensoid solution it exerts a protective action, preventing or hindering the precipitation of the suspensoid by electrolytes.

EXPERIMENT. (a) To 5 c.c. of N/20 silver nitrate solution add three drops nitric acid and 5 c.c. of N/20 sodium chloride; a curdy precipitate is obtained.

(b) Into one test-tube put 5 c.c. N/20 silver nitrate, 3 drops nitric acid and about 1 c.c. gelatin. Into another put 5 c.c. NaCl and 1 c.c. gelatin. Empty both simultaneously and at the same rate into a beaker. An opalescent solution (milky) which resembles glycogen solution, but no precipitate, is obtained. Now dilute and note carefully absence of precipitate.

Photographic plates are made by taking advantage of the protective action of gelatin, preventing precipitation of the silver salt.

The therapeutic agent, *collargol*, is said to be a colloidal silver preparation, in which albumin acts as the protective agent. There being no Ag ions it is not toxic; bacterial action, however, changes it to ordinary silver and the ions act antiseptically.

There is good reason for believing that enzymes are colloidal substances.

SURFACE TENSION.

The molecules of a liquid are attracted to one another in all directions, these attractions neutralizing one another. At the surface, however, the molecules are attracted towards the middle of the liquid and there is no counter-balancing attraction in the opposite

direction, thus there results a definite pressure called surface tension. In the case of solutions there is a greater concentration of the solute at the surface than elsewhere. The pressure crowds the molecules closer together. Surface tension is equivalent, then, to the stretching of an elastic membrane at the surface. Fine powders of such a nature that they do not readily take up moisture (as sulphur) float when sprinkled on water—the particles rest on the surface exactly the same as if on a membrane. If the surface tension be lowered as results when bile salts are dissolved in the water, such particles will not be buoyed up, but will sink. Many organic liquids such as methyl and ethyl alcohols, ether, chloroform, glycerol, acetone, aniline, pyridine, phenol and many organic acids, have a low surface tension; on the other hand when they are dissolved in water they lower the surface tension of the water.

EXPERIMENT. (a) Fill a test-tube with water, another with 1% solution of castile soap; on the surface of each liquid dust a few very fine particles of sulphur. The sulphur readily sinks in the soap solution. Dilutions of the soap may be made to find how dilute a solution still shows marked lowering of surface tension.

(b) Dip capillary tubes in various liquids, as water, alcohol, soap solution, etc. The height to which the liquid rises (more accurately the weight of liquid raised) is a measure of the surface tension.

In similar manner within a liquid containing colloidal or suspended particles, there is a surface of the liquid

presented to the surface of each particle and hence surface tension comes into play. Thus in the region of each colloidal particle there is a minute surface tension area surrounding it. How important this is in a consideration of colloidal solutions will be understood by calling attention to the enormous increase of surface exposure when a substance is divided into fine particles. A compact sphere of substance one mm. in diameter (surface area of 0.0314 sq.cm.), if broken up into particles of uniform size, corresponding to the size of the largest suspensoid particles (0.1μ), will acquire a surface area of 314 sq.cm. If a colloidal solution be purified, that is, freed of other dissolved substances, the surface tension about the particles becomes higher, and as it becomes higher, the difference in potential increases and the particles divide into smaller particles. When an electrolyte is added to the solution, it concentrates at the surfaces between solvent and colloidal clumps, just as it concentrates at the surface in contact with air (as above). The electrical charge of the electrolyte opposes the force of surface tension and lessens it. Surface tension being lessened the colloidal particles aggregate more and more so as to restore the balance in potential.

Suspensoid particles attract ions of opposite electrical charge and hold them, so that when the colloid is precipitated the ions are carried down also. This holding is not chemical union, but condensation of a substance at the surfaces of contact and is called **adsorption**. So also two colloids of opposite electrical charge will hold one another by adsorption and precipitate together. One of the colloids may be an emul-

soid; the suspensoid and emulsoid adsorb and then when an electrolyte is added the suspensoid is precipitated, and the adsorbed emulsoid is carried down with it. For example if $\text{Fe}(\text{OH})_3$ (electropositive) be mixed with a faintly alkaline solution of protein (electronegative), on adding a salt both iron and protein are completely precipitated.

EXPERIMENT. To 10 c.c. of blood serum add 70 c.c. of water, then 15 c.c. of colloidal ferric hydroxide solution (Merck's dialyzed iron containing 5% Fe_2O_3), shake, add powdered sodium sulphate, shaking after each addition, until a gelatinous precipitate forms. Filter, test the filtrate for protein (biuret test, p. 228).

Adsorption can occur independently of electrical considerations. In this case it is to be explained solely by the concentration of the adsorbable substance at colloidal surfaces and the lowering of surface tension of the liquid about the colloidal particles.

The use of animal charcoal to remove coloring matters and certain other substances from solutions is a case of adsorption.

Ferments readily adsorb to colloids. There is a surface condensation of the enzyme on the colloid particles. This is not selective, for an enzyme can adsorb to substances on which it has no action. Recent investigation seems to show that the rate of enzyme action at any particular moment is proportional to the amount of enzyme present in the adsorbed state at that moment.

VISCOSITY.

The viscosity of a liquid depends upon its internal friction. A measurement of this friction may be made by observing the time required for a certain quantity of liquid to pass through a capillary tube and comparing with the time required by an equal volume of water in the same apparatus. For accurate work the temperature must be carefully regulated.

We may suppose that the layer of liquid in contact with the wall is not moving, that the next layer is moving slowly, and that each layer moves faster the nearer it is to the centre of the tube. The rate of flow of the liquid as a whole will depend upon the amount of friction between these successive layers, hence measurement of this rate gives a basis for calculating viscosity. When liquid particles push past each other in this way work must be done and the amount of work necessary is dependent upon the internal friction.

Specific viscosity is the ratio of the viscosity of a liquid to that of another liquid which has been chosen as a standard. Comparing with water as unity the specific viscosity (at 25°) of five per cent ethyl alcohol is 1.161 and of five per cent ethyl acetate is 1.044.

EXPERIMENTS. (1) Compare the viscosity of water, of absolute alcohol and of 50% alcohol successively in an Ostwald viscosity pipette. To do this pour about 5 c.c. of the liquid into the large tube and by suction from a suction pump draw it into the small tube and bulb, filling above the upper mark, disconnect and prevent the liquid flowing back by sealing the end with the finger (as in using a pipette), draw

off the excess of liquid in the large tube with a pipette. Now releasing the finger start a stop-watch at the instant that the meniscus reaches the upper mark and stop the watch when it reaches the mark on the capillary tube. The dilute alcohol has a greater viscosity than either water or absolute alcohol.

(2) Use a viscosimeter such as is used for commercial chemical work; Scott's is a simple apparatus. Try this with water and later with an oil at the same temperature, repeat the experiment, using a temperature 20° higher. Each determination is made as follows; put 200 c.c. of the liquid into the viscosity cup, set a graduate under the cup to catch the outflow, press the lever which raises the plunger and at the same instant start the watch, when 50 c.c. has flowed out stop the watch and let the plunger fall. Dividing the time for the oil by the time for water gives the figure for the specific viscosity of the oil.

Suspensoid colloidal solutions have a viscosity but slightly different than it would be if the colloidal particles were not present. Emulsoid colloidal solutions, however, show marked increase of viscosity if their concentration is above one per cent.

Traces of acid or of alkali distinctly increase the viscosity of some emulsoids. There is a point of maximum viscosity, for example with gelatine solution the maximum viscosity with HCl is secured when $\frac{N}{256}$ is present. A concentration of alcohol below that necessary to cause precipitation (as 35%) increases the viscosity of albumin solutions.

Increase of temperature lessens viscosity.

MOLECULAR WEIGHT DETERMINATION BY ANALYSIS
OF DERIVATIVES.

The molecular weight of a substance can also be deduced from a *quantitative analysis of its derivatives*. This method is most easily applied to acids and bases. Take, for example, a simple acid, such as acetic. By analysis, its formula might be CH_2O , or any multiple thereof. By forming its silver salt and estimating the amount of silver in it, this will be found to be 64.6%. Now, knowing that the atomic weight of silver is 107.9 and that it is monovalent, and having ascertained that only one silver acetate occurs (showing that the acid is monobasic), we can see what formula agrees with this proportion of silver in silver acetate. Suppose this salt to have the formula

CHOAg , then the % of Ag must be $\frac{107.9}{136.9} \times 100 = 78.8$.

Obviously CH_2O cannot be the correct formula for acetic acid. If we take $\text{C}_2\text{H}_3\text{O}_2\text{Ag}$ as the formula,

the per cent of silver will be $\frac{107.9}{166.9} \times 100 = 64.6\%$,

therefore $\text{C}_2\text{H}_4\text{O}_2$ is the correct formula. In the case of bases, their chlorplatينات have been found to be the most suitable compounds to form for this purpose.

CHAPTER V.

FORMULÆ, EMPIRICAL AND STRUCTURAL. ISOMERISM.

A KNOWLEDGE of the percentage composition and of the molecular weight of a substance, as we have seen, enables us to assign to it a formula indicating the number of atoms of each element present in the molecule. This is called the *empirical formula*. But it often happens that several organic substances with very different properties may have the same empirical formula. For example, there are no fewer than eighty-two compounds having the empirical formula $C_9H_{10}O_3$. Such bodies having the same empirical formula are called isomers. It is evident, therefore, that a more detailed formula is necessary—a formula, namely, in which the relations of the various atoms to one another (i.e., the grouping of the atoms) are indicated. Such a formula is called the *structural formula*. It is ascertained by acting on the substance with reagents which decompose it into simple bodies that can be identified; in other words, we must tear the molecule apart. After some knowledge has been gained as to what simpler groups of atoms the body is composed of, an attempt is made to build up the substance by causing the simpler groups to unite together, i.e., by synthesizing the sub-

stance. If the synthesis is successful, the structure of the molecule is proven.

We see then that the structural formula is not only a graphical expression of the actual number of the various atoms present in a molecule of the substance, but it is also an epitome of the more important reactions of the substance.

In the chapters which immediately follow this one, the methods by which the various facts indicating the structure of the molecule are discovered will be fully explained (see especially acetic acid, p. 140). When we come to study the more complex substances, we shall find that even the structural formula does not always suffice to differentiate the substance, since, indeed, there may be several bodies having the same structural formula. In such cases it is supposed that the cause of the difference lies in the order of arrangement of the atoms in space. This subject will be found described in connection with lactic and tartaric acids (pp. 198 and 206).

Before starting with a systematic study of the compounds of carbon the student should bear in mind the extreme importance of the structural formula; he should never allow one to pass him without thoroughly understanding why it is so written. If he conscientiously follows this advice, he will soon find that organic chemistry is by no means the uninteresting and disconnected subject so many students think it to be.

SYNOPSIS OF CHAPTERS I-V.

Determination of the Chemical Character of an Organic Compound.**1. PURIFICATION.**

- (a) Methods.
- (b) Tests of purity.

2. IDENTIFICATION.

- (a) Physical properties.
- (b) Elementary analysis.

3. EMPIRICAL FORMULA.

- (a) Elementary analysis.
- (b) Molecular weight determination.

4. STRUCTURAL FORMULA.

- (a) Reactions to detect presence and relative placing of atoms and groups of atoms in the molecule.
- (b) Synthesis of the molecule.

CHAPTER VI.

PRELIMINARY SURVEY OF ORGANIC CHEMISTRY.

BEFORE attempting to study the various organic substances individually, it is essential that we possess a general idea of their relationships to one another. Their number is so great that, did we attempt to remember the properties and reactions of each organic substance separately, we should utterly fail, and should, moreover, probably overlook one of their most important characteristics in contrast with inorganic substances, viz., their transmutability into other organic compounds. In inorganic chemistry it is impossible to convert the compounds of one element into those of another element, except by substituting the elements. Each element has its own fixed chemical properties and compounds. In organic chemistry, on the other hand, as remarked above, we may consider all our substances as compounds of the element carbon and as being, therefore, convertible into one another.

As is natural, we select as our basis of classification the very simplest organic substances, namely, those which contain carbon along with one other element. From our studies in inorganic chemistry we know that there are several elements with which carbon may be thus combined, e.g., with oxygen in CO_2 , with

sulphur in CS_2 , etc. We do not, however, consider these as organic compounds, the simplest organic compounds being those in which carbon is combined with hydrogen or with nitrogen.

In union with nitrogen, carbon forms *cyanogen* (CN (in the free state C_2N_2), which is the lowest member of a group of compounds including hydrocyanic acid, HCN , cyanic acid, HCNO , sulphocyanic acid, HCNS) and the substituted ammonias.

In union with hydrogen, carbon forms the so-called *hydrocarbons* (i.e., hydro(gen) carbons). Practically all the remaining carbon compounds may be considered as derived from these.

The quantitative relationship between C and H in hydrocarbons is variable, so that we are enabled to subdivide hydrocarbons into several groups. If we express the hydrogen in terms of its proportion to carbon, we shall find that all the hydrocarbons group themselves into several series, four of which are of importance. The general formulæ for the four series or groups are as follows:



(n designating the number of C atoms).

It will, moreover, be found that it is to the first and fourth of these groups that the great majority of hydrocarbons belong.

If, now, we investigate the behaviour of the members of these four groups towards hydrobromic acid, we shall find that members of the first and fourth groups do not readily react, whereas those of the second and third do;

indeed, that these directly combine with the reagent by addition, i.e., without chemical substitution. We may, therefore, further subdivide our four groups into two, viz., *saturated* (1st and 4th) and *unsaturated*¹ (2d and 3d).

Of the two *saturated* groups it will be found that many members of the 4th group have an aromatic odour, whereas those of the 1st do not. The members of the 4th group are hence often styled *aromatic compounds*, and on account of the fact that the members of the 1st group are very resistant towards chemical reagents they are called *paraffins* (*parum affinis*).

On account of their properties, then, we may amplify our classification into paraffins (1st group), unsaturated compounds (2d and 3d), and aromatic bodies (4th).² Compounds of the first three groups make up the ALIPHATIC OR FATTY DIVISION of organic chemistry.

The compounds and derivatives formed by the various hydrocarbons of each of these groups are, in general, analogous, although the reactions by which they are produced may differ somewhat. If we understand the chemistry of the most important derivatives of one hydrocarbon in each group we shall be able to infer approximately what the derivatives and reactions of all the other members of the group will be; and further, when we come to study the hydrocarbons of the other groups we shall find many of their compounds quite similar to those already met with.

From these preliminary remarks it will be evident that

¹ Only unsaturated compounds can form addition products.

² The groups are also sometimes named from the lowest member of each, e.g., methane group, benzene group, etc.

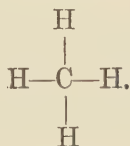
we must first of all take one group, and, having shown the relationship of its various members to one another, then study carefully the derivatives of some one or two of these members.

Let us take the **paraffins**. They have the general formula C_nH_{2n+2} . The following is a list of the most important members:

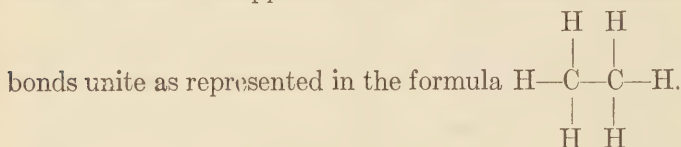
Methane, CH_4	Butane, C_4H_{10}
Ethane, C_2H_6	Pentane C_5H_{12}
Propane, C_3H_8	Hexane, C_6H_{14}

It will be noticed that each differs from the one preceding it by CH_2 . They all form the same kind of derivatives, differing from one another again by CH_2 ; thus the hydroxide or alcohol of methane has the formula CH_3OH , and of ethane C_2H_5OH . Such a series is called an *homologous series* (*cf.* nitrogen oxides series).

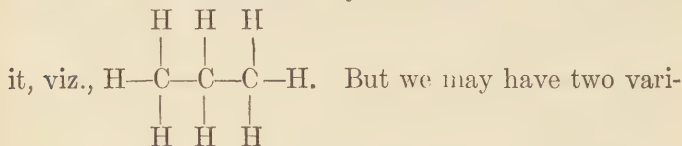
Let us consider why it should be that the increase of complexity is by CH_2 . To understand this we must remember that C is considered to have a valence of four; that, in other words, an atom of it can combine with four atoms of a monovalent element such as H, and that each of these valence bonds has exactly the same combining value. We may therefore write the structural formula for methane as



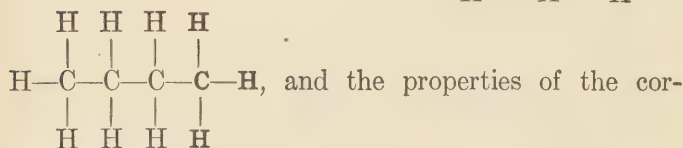
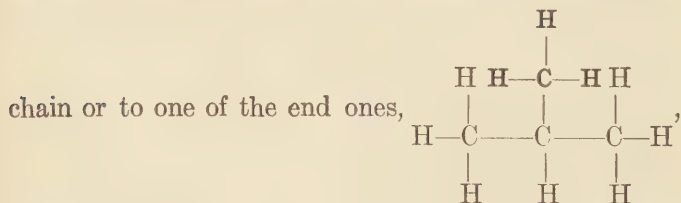
When two methane molecules fuse together a hydrogen atom of each disappears and the liberated valence



Since each of the four valence bonds of C has the same value it will be obvious that only one propane can exist: that we can write only one structural formula for



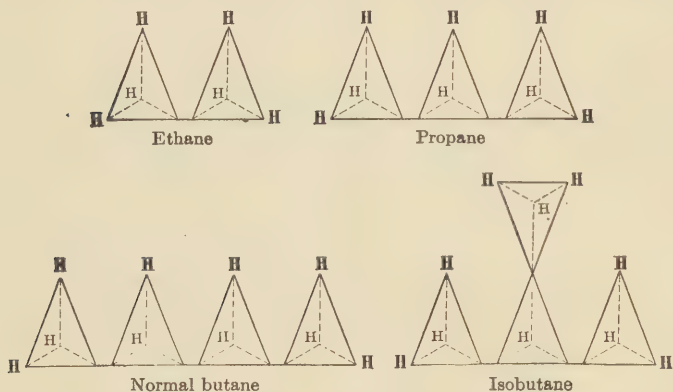
for, in adding an extra CH_3 group to propane, we may add it either to the central C atom of the



responding body will vary accordingly; in other words, it makes a difference when the extra CH_3 group is tacked on to a C atom in union with two H atoms (as is the case with the central atom), and when on to one with three H atoms (as in the case of an end atom).

When the substitution occurs in the centre of the chain the resulting body is called an *iso*-compound; when at the end it is *normal*. Such an *iso*-compound therefore contains a branched chain. Now, this *isomerism* applies not only to the methyl derivatives of propane—for butane may be considered as such—but also to all its derivatives, e.g., chlorides, hydroxides, etc.

By using models instead of formulæ these points can be still more clearly demonstrated: thus we may consider C as occupying the core of a tetrahedron (made



of wood), the four solid angles of which represent monovalent combining affinities, these angles being covered in the model by pyramidal tin caps representing H atoms (see fig. 22, p. 206). By removing an H cap from two models of methane and joining the two tetrahedra together by the bared angles we obtain the model of ethane. And if by removing another H cap from ethane we unite three such tetrahedra we obtain the

model of propane. It does not matter which of the H caps we remove in these manipulations; the resulting ethane or propane models are always the same. When we proceed to add another tetrahedron to propane, however, it will be evident that this can be done in either of two ways, by attaching it either to one of the end tetrahedra or to the central one; in the former case the model will represent normal butane, and in the latter isobutane; and so with the other homologues.

We may also describe this progression from one hydrocarbon to the next higher as being due to the replacement of the H atoms of the former by the group CH_3 , called *methyl*.

Now we may proceed with the **derivatives of the paraffins**. These are produced by the replacement of one or more of the H atoms of the simple hydrocarbons by various elements or groups of elements. Since, as explained, these derivatives are, in general, the same for each member of a series, we may choose any one of these and confine our attention for the present to its derivatives, remembering always that the corresponding derivative of any other member of the series will differ from it by just as many CH_2 groups as did the original hydrocarbons differ from one another.

In inorganic chemistry the halogen compounds, the oxides, and the hydroxides are among the most important compounds of an element, and the same applies to the hydrocarbons: each has halogen derivatives, oxides (ethers), and hydroxides (alcohols). Beyond these, however, the analogy breaks down, for whereas an inorganic hydroxide is an ultimate product and cannot be further oxidized, an organic hydroxide (or

alcohol) can be oxidized so as to yield various substances according to the extent of the oxidation and the nature of the alcohol started with. We may, therefore, classify our derivatives thus:

Halides.

Oxides or ethers.

Hydroxides or alcohols.

Oxidation products of alcohols.

Halides. When the paraffins are brought into contact with chlorine, substitution of one or more of the H atoms occurs. Thus, taking methane, we may have monochlormethane, dichlormethane, trichlormethane (chloroform), and tetrachlormethane. In connection with the monohalogen substitution products it should be pointed out that they may be considered as derived from a halogen acid, the H of the acid having been replaced by a hydrocarbon minus one of its H atoms. The general term for all such groups is *alkyl*, and the specific names for the alkyls are methyl (CH_3 -), ethyl (C_2H_5 -), propyl (C_3H_7 -), and so on. An alkyl is, therefore, analogous with a monovalent element or with NH_4 .

Halogen atoms may likewise displace one or more of the H atoms of the alkyl radicle when this latter is already in combination with some other substituting group. Thus, chloral is trichloraldehyde, CCl_3CHO , aldehyde being CH_3CHO .

Oxides (or ethers). Since oxygen combines with two atoms of a monovalent element, as in sodium oxide, Na_2O , the lowest alkyl oxide will have the formula

$\begin{array}{c} \text{CH}_3 \\ \diagup \\ \text{CH}_3 \end{array} \text{O}$. To this group belong the ethers, common ether being $\begin{array}{c} \text{C}_2\text{H}_5 \\ \diagup \\ \text{C}_2\text{H}_5 \end{array} \text{O}$.

Hydroxides (or alcohols). When one of the H atoms of methane is replaced by hydroxyl, OH, methyl alcohol

is formed. Thus $\begin{array}{c} \text{H} \\ | \\ \text{H}-\text{C}-\text{H} \\ | \\ \text{H} \end{array}$ becomes $\begin{array}{c} \text{H} \\ | \\ \text{H}-\text{C}-\text{OH} \\ | \\ \text{H} \end{array}$, and

it does not matter which of the H atoms is thus replaced, the resulting compound being always the same.

The same is true for ethane and its alcohol, ethyl alcohol, $\text{CH}_3-\text{CH}_2\text{OH}$.

When we come to form the alcohol from propane, however, we encounter conditions analogous with those which exist when butane is formed from propane (see p. 84); we may add the OH group to a C atom of propane which is in combination with three hydrogen atoms or to one in union with two such, and the resulting product, as we have seen, will exhibit different properties. Consequently we have two forms of propyl alcohol. Of these the OH group in the one is attached at the end of the chain, $\text{CH}_3-\text{CH}_2-\text{CH}_2\text{OH}$; in the other it is attached in the middle of the chain,

$\begin{array}{c} \text{OH} \\ | \\ \text{CH}_3-\text{CH}-\text{CH}_3 \end{array}$ The former is called a *primary alcohol*, the latter a *secondary alcohol*.

In the case of butane, we may have the hydroxyl radicle at the end of the chain, $\text{CH}_3-\text{CH}_2-\text{CH}_2-\text{CH}_2\text{OH}$ (primary butyl alcohol); or attached to a C atom in the

centre of the chain with one other H atom attached to it, $\text{CH}_3\text{—CH}_2\text{—CH}$ $\begin{smallmatrix} \text{OH} \\ \diagup \\ \text{CH}_3 \end{smallmatrix}$ (secondary butyl alcohol); or—a third possibility—the hydroxyl radicle may be attached to a C atom which is not directly combined

with any other H atom, thus $\text{CH}_3\text{—C—OH}$ $\begin{smallmatrix} \text{CH}_3 \\ | \\ \text{CH}_3 \end{smallmatrix}$ (tertiary butyl alcohol).

There are, therefore, three varieties of these alcohols:

1. Primary, containing the group $\text{—CH}_2\text{OH}$
2. Secondary, “ “ “ —CHOH—
3. Tertiary, “ “ “ $\begin{smallmatrix} | \\ \text{—C—OH} \\ | \end{smallmatrix}$

The essential chemical difference between these is that when oxidized they yield different products. These we shall consider immediately.

In all these alcohols only one hydroxyl radicle is present: they are analogous with hydroxides of monovalent elements such as sodium (thus NaOH is analogous with CH_3OH). Just as in inorganic chemistry, however, we may have hydroxides with two hydroxyls, e.g., Ca $\begin{smallmatrix} \text{OH} \\ \diagup \\ \text{OH} \end{smallmatrix}$, so may we have alcohols with two

hydroxyls, e.g., $\begin{smallmatrix} \text{CH}_2\text{—OH} \\ | \\ \text{CH}_2\text{—OH} \end{smallmatrix}$. Similarly, there are alcohols containing three hydroxyl groups, e.g., $\begin{smallmatrix} \text{CH}_2\text{—OH} \\ | \\ \text{CH—OH} \\ | \\ \text{CH}_2\text{—OH} \end{smallmatrix}$

which are analogous with Al $\begin{smallmatrix} \text{OH} \\ \diagup \\ \text{—OH} \\ \diagdown \\ \text{OH} \end{smallmatrix}$.

Alcohols, like hydroxides in general, have the power of neutralizing acids to form salts. Thus, sodium hydroxide reacts with HCl in accordance with the equation $\text{NaOH} + \text{HCl} = \text{NaCl} + \text{H}_2\text{O}$: and taking an alkyl hydroxide (alcohol) instead of an alkaline hydroxide, we have $\text{ROH} + \text{HCl} = \text{RCl} + \text{H}_2\text{O}$ ($\text{R} = \text{alkyl}$).¹ They can react in this way with organic acids, the resulting body being known as an ethereal salt or ester (see p. 150). These organic salts differ widely from metallic salts in their chemical behaviour.

An alcohol with only one hydroxyl group is called *monacid*,² because it can react with only one molecule of a monobasic acid; those with two such groups are called *diacid*; those with three are called *triacid*. The monacid alcohols are by far the most numerous; there is only one diacid alcohol (glycol) of importance and one triacid alcohol (glycerol).

Oxidation Products of Alcohols. As has been mentioned (p. 88), the division into primary, secondary, and tertiary alcohols is warranted by the difference of their behaviour on oxidation.

Primary alcohols yield on oxidation aldehydes and acids.

Secondary alcohols yield ketones.

Tertiary alcohols, when oxidized, break up into lower compounds.

The oxidation products that we must consider are, therefore, aldehydes, acids, and ketones.

A. Aldehydes. When methyl alcohol, CH_3OH , is oxidized, one of the H atoms of the methyl radicle

¹ Alcohols, however, are not really basic in the same sense as are metallic hydroxides.

² The terms *monatomic* and *monohydric* are also used.

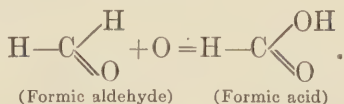
becomes replaced by hydroxyl, so that a body having the formula $\text{CH}_2(\text{OH})_2$ would tend to be formed. But such a body having two hydroxyls directly attached to a C atom cannot exist, and it immediately breaks up, giving

off water, thus: $\text{H}-\overset{\text{H}}{\underset{\text{O}}{\text{C}}}\begin{matrix} \nearrow \text{O} \text{H} \\ \searrow \text{O} \text{H} \end{matrix}$, leaving a body having the

formula $\text{H}-\overset{\text{H}}{\text{C}}=\text{O}$. This is an aldehyde, and the group

$-\overset{\text{H}}{\text{C}}=\text{O}$ is known as the *aldehyde group*. The CO portion of this group is called *carbonyl*. Each hydrocarbon has a corresponding aldehyde.

B. Acids. When an aldehyde is further oxidized it absorbs oxygen and forms a body having the group COOH , which is called the *carboxyl group* (from carb[onyl hydr]oxyl) and is the characteristic acid group of organic compounds:



The H atom of this carboxyl group can be replaced by an atom of a monovalent metal to form a salt, thus: $\text{H} \cdot \text{COONa}$, sodium formate. Instead of a metal, an alcohol may replace this H atom, the resulting compound being called an ethereal salt, thus: $\text{H} \cdot \text{COOC}_2\text{H}_5$, ethyl formate. Such an acid can form only one salt; it is *monobasic*.

If two carboxyl groups be present the resulting acid is *dibasic*. The lowest dibasic acid corresponding to the simplest diacid alcohol is oxalic, having the formula

$\begin{matrix} \text{COOH} \\ | \\ \text{COOH} \end{matrix}$. Like dibasic acids in general, these acids

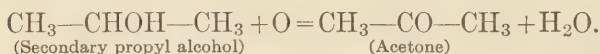
can form two series of salts, in one of which only one

carboxyl group reacts, $\begin{array}{c} \text{COOK} \\ | \\ \text{COOH} \end{array}$ (acid potassium oxalate),

and in the other, both, $\begin{array}{c} \text{COOK} \\ | \\ \text{COOK} \end{array}$ (neutral potassium oxalate).

Tribasic organic acids also exist, but are unimportant.

C. Ketones. When a secondary alcohol is oxidized it forms a body having the group —CO— , which is called a ketone:



THE NITROGEN DERIVATIVES are divided into three classes—cyanogen, ammonia, and nitro-compounds.

As we have inorganic cyanides, as KCN, so we have **organic cyanides**, as $\text{CH}_3\cdot\text{CN}$, methyl cyanide.

There are several kinds of **ammonia derivatives**. One hydrogen atom of NH_3 may be replaced by an organic radicle, leaving the group NH_2 , which is called the *amido- or amino-group*. Two hydrogen atoms may be displaced, leaving NH , called the *imido-group*. All three hydrogen atoms may be displaced, leaving only N; such compounds are called *tertiary bases*. Or we may have the hydrogens of ammonium (NH_4) in NH_4OH displaced, as in the *quaternary bases*.

Several organic **nitrites** are of importance.

SULPHUR DERIVATIVES. In these, sulphur may take the place of oxygen in an alcohol or ether, giving **sulphur alcohols** (mercaptans), as CH_3SH , and **sulphur ethers**, as $\text{CH}_3\text{—S—CH}_3$.

Sulphonic acids contain the group SO_3H instead of carboxyl.

AS MIXED COMPOUNDS we class (1) hydroxy-acids, (2) amino-acids, acid amides, and certain complex amido- and imido-compounds, and (3) carbohydrates.

The **hydroxy-acids** contain one or more hydroxyls besides that in carboxyl.

The **amino-acids** contain both the NH_2 and COOH groups. **Acid amides** have the OH of carboxyl substituted by an NH_2 group.

The **carbohydrates** are complex compounds containing alcohol groups. Many have an aldehyde or ketone group.

Finally, **UNSATURATED HYDROCARBONS**, having the linkings $\text{C}=\text{C}$ and $\text{C}\equiv\text{C}$, and their derivatives, will conclude the chemistry of fatty compounds.

The last great division of organic chemistry, that of the **AROMATIC OR BENZENE COMPOUNDS**, can be considered but briefly in this book.

SYNOPSIS.

I. Fatty or Aliphatic Compounds.

A. SATURATED HYDROCARBONS.

Paraffins, C_nH_{n+2} .

Paraffin derivatives.

1. *Halogen substitution products.*

2. *Oxides or ethers.*

3. *Hydroxides or alcohols.*

a. Monacid alcohols.

(1) Primary alcohols, group $-\text{CH}_2\text{OH}$.

Oxidation products { Aldehydes, $-\text{CHO}$.
Acids, $-\text{COOH}$.

(2) Secondary alcohols, $-\text{CHOH}$.

Oxidation product { Ketones, $-\text{CO}-$.

(3) Tertiary alcohols, —COH .

b. Diacid alcohols.

Oxidation products { Aldehydes.
Acids.

c. Triacid to hexacid alcohols.

Oxidation products { Aldehydes.
Acids.

4. *Nitrogen derivatives.*

a. Cyanogen combinations.

b. Ammonia combinations (amido-group, NH_2 ; imido-group, NH , etc.).

c. Nitrites.

5. *Sulphur derivatives.*

6. *Mixed compounds.*

a. Hydroxy-acids.

b. Amino-acids, acid amides, and other similar compounds.

c. Carbohydrates.

B. UNSATURATED HYDROCARBONS.

1. *Ethylenes*, C_nH_{2n} (—C=C—).

2. *Acetylenes*, $\text{C}_n\text{H}_{2n-2}$ ($\text{—C}\equiv\text{C—}$).

C.¹

II. Aromatic Compounds.²

A. BENZENE HYDROCARBONS, $\text{C}_n\text{H}_{2n-6}$.

aromatic derivatives (see synopsis, p. 380).

¹ As will be explained later, the group of cyclic hydrocarbons and the terpenes (see p. 275) is really an intermediate class of compounds between the fatty and the aromatic, and it would naturally be inserted in the synopsis after C. To avoid confusion we say nothing about these compounds in this chapter.

² A more scientific classification of organic compounds groups fatty compounds as *acyclic* (not closed chain structure), benzene derivatives as *isocyclic* (closed chain of C atoms), and certain other aromatic compounds as *heterocyclic* (closed chain in which N, S, or O takes the place of one of the C atoms of the chain).

CHAPTER VII.

SATURATED HYDROCARBONS. THE METHANE SERIES.

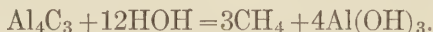
METHANE (CH_4) can be synthesized from the elements in several ways:

(1) A small quantity of CH_4 can be produced directly from the elements by passing a stream of hydrogen between the glowing carbon tips of an electric arc-light (see acetylene, p. 273).

(2) By producing carbon disulphide (CS_2) and hydrogen sulphide (H_2S), and allowing a mixture of them to act on heated copper:



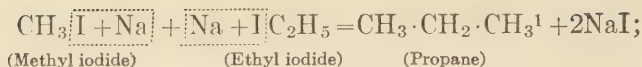
(3) By the action of water on aluminium carbide:



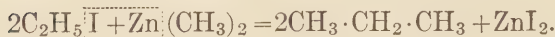
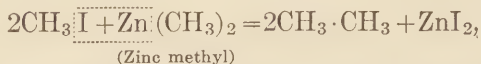
THE PARAFFINS OR MARSH-GAS SERIES, $\text{C}_n\text{H}_{2n+2}$.

Having obtained methane, the other members of the series may be built up from it by first of all producing its halogen substitution products and then reacting on these with metals, thus:

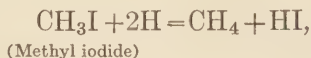




also with zinc methyl, thus:



The paraffins may be prepared for general purposes (1) by decomposing the proper substitution product with nascent hydrogen,² or (2) by heating an acid derivative with an excess of soda-lime:



Methane (marsh-gas), CH_4 , occurs in nature as a gas arising from stagnant water where decomposition of vegetable matter is going on, as fire-damp in coal-mines, and as one of the constituents of natural gas. Its production by decomposition of vegetable matter can be brought about in the laboratory by inoculating

¹ C_2H_6 and C_4H_{10} are also formed.

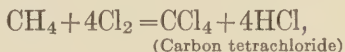
² The nascent hydrogen for such reactions as this may be obtained from a copper-zinc couple (made by heating together one part of powdered copper with three parts of powdered zinc and then cooling in a closed vessel). In the presence of a trace of acid (H_2SO_4) the couple readily yields nascent hydrogen. In the above reaction a mixture of the methyl iodide with alcohol and a drop of H_2SO_4 is brought into contact with the couple, drop by drop.

water containing small suspended pieces of filter-paper (cellulose) with the microorganisms contained in sewage. It forms an explosive mixture with air, hence the danger of having bare flames in coal-mines and the necessity for using the Davy safety-lamp. Fortunately the kindling temperature (i.e., the temperature at which it explodes) of this gas is high.

Natural gas has about ninety-five per cent methane; it also contains a little nitrogen, ethane, hydrogen and only a trace of carbon monoxide. There are two hypotheses as to the production of natural gas, one that it is the result of decomposition of vegetable or animal matter, and the other that it is due to the action of water on metallic carbides (*cf.* aluminium carbide reaction). *Coal-gas* contains about forty per cent of methane.

Water-gas is the most poisonous illuminating gas that is used, because of its large content of carbon monoxide. Coal gas is also very dangerous, containing four to ten per cent of carbon monoxide. This poison acts by combining with the hæmoglobin of the blood, thus interfering with the oxygen-carrying power of the blood. *Pintsch gas* (produced from oil) contains very little carbon monoxide, but a large amount of methane and other hydrocarbons.

Methane is a colourless, odourless, stable gas. When mixed with chlorine and exposed to direct sunlight it explodes:



or when exposed to diffused sunlight it forms a mixture of monochlor- (CH_3Cl), dichlor- (CH_2Cl_2), trichlor-

(CHCl_3), and tetrachlor-methane (CCl_4). The last is also called carbon tetrachloride.

EXPERIMENT. Dehydrate some sodium acetate by heating it in an evaporating dish with a small flame. Cool, mix 10 gm. with 10 gm. of soda-lime, and heat in an iron retort. A large test-tube could be used instead of a retort. By means of a delivery tube fitted to the retort, collect the evolved methane over water in the usual manner. Test its inflammability, also its lightness compared with air.

Ethane (C_2H_6), **propane** (C_3H_8), and **butane** (C_4H_{10}) are also gases at ordinary temperatures. The other paraffins are liquids or solids. Above butane the name indicates the number of carbon atoms in the formula. There is a regular gradation of physical properties from the lowest to the highest members of the paraffin series: the boiling-point, the specific gravity, and the melting-point increase as we ascend the series.

	Boiling-point.	Specific gravity.	Melting-point.
Methane, CH_4	-164°	0.415 (at -164°)	-184°
Ethane, C_2H_6	-84.1°	0.446 (at 0°)	-172.1°
Propane, C_3H_8	-44.5°	0.535 (at 0°)	-45°
Butane, C_4H_{10}	$+1^\circ$	0.600 (at 0°)	
Pentane, C_5H_{12}	36.3°	0.627 (at 14°)	
Hexane, C_6H_{14}	69°	0.6603 (at 20°)	
Tetradecane, $\text{C}_{14}\text{H}_{30}$	252°	0.775 (at 4°)	4°
Hexadecane, $\text{C}_{16}\text{H}_{34}$	287°	0.7758 (at 18°)	18°
Octodecane, $\text{C}_{18}\text{H}_{38}$	317°	0.777 (at 28°)	28°

The heat of combustion of a gram molecule of a paraffin hydrocarbon is about 158 large calories greater than that of the next lower hydrocarbon; this is the heat of combustion value of the CH_2 group.

The members of the series after methane are met with mainly in petroleum. American petroleum also contains a few sulphur derivatives. California petroleum contains some benzene hydrocarbons. To render petroleum suitable for commercial purposes, it is subjected to crude fractional distillation. The oils thus obtained are purified by successive treatment with sulphuric acid, caustic soda solution, and water. The lower fractions are distilled with steam; the distillate between 40° and 150° is *gasoline* (or *naphtha*), and that between 150° and 300° is *kerosene*. Gasoline and its products are mostly mixtures of C_6H_{14} , C_7H_{16} , and C_8H_{18} . From low-boiling gasoline can be obtained, by careful fractional distillation, cymogene (a gas), rhigolene (b. pt. 18.3°), *petroleum ether* ($40-70^{\circ}$), gasoline ($70-90^{\circ}$), *naphtha* ($80-110^{\circ}$), *ligroin* ($80-120^{\circ}$) and *benzine* ($120-150^{\circ}$). High-boiling gasoline, called also *benzine*,¹ is used as a solvent in many industrial processes. Kerosene contains the paraffins from C_9H_{20} to $C_{16}H_{34}$. It should contain no gasoline, as the vapour of the lower hydrocarbons in a lamp would form an explosive mixture with air. Its flashing-point, tested in a manner similar to that described in the experiment below, tells us whether it contains any gasoline. The minimum flashing-point is regulated by law, varying in different states and countries from about 38° to 49° . The residue, after kerosene is removed, may be filtered, separating vaseline from lubricating oil, or it may be distilled, on cooling the distillate (paraffin oil) paraffin separates out, the liquid

¹ Carefully distinguish from *benzene* (p. 283).

left is used as a lubricating oil. *Vaseline* is a yellowish semi-solid product, while the commercial substance called *paraffin* is a white solid. Pennsylvania petroleum yields 16.5% naphtha, 54% kerosene, 17% lubricating oils, 2% paraffin and 10% coke. The fuel value of gasoline is greater than that of an equal weight of kerosene, because of the greater percentage of hydrogen present.

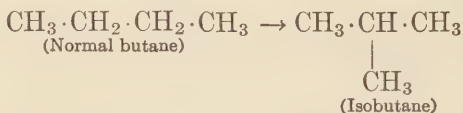
EXPERIMENT. Place the flashing-point apparatus (see fig. 18) containing 20 c.c. of kerosene in a large beaker two-thirds full of water. Suspend a thermometer so that the bulb is in the kerosene. Heat the beaker slowly. Bubble air through the oil at frequent intervals, and test the vapour with a lighted match. Note the temperature when the *vapour* takes fire (the burning temperature of the oil is 40°–50° above the flashing-point).



FIG. 18.

There are many isomers of the paraffins (see p. 84). These *iso-compounds* are represented in their formulæ as having branched chains of carbon atoms instead of straight chains as in the normal compounds, and they possess properties quite different from those of the normal paraffins.

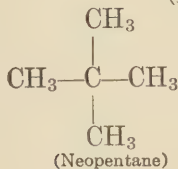
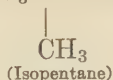
Isobutane is the iso-compound having the fewest carbon atoms (see p. 84):



Isopentanes. There are several pentanes:



(Normal pentane)



The newer nomenclature designates these isomers as derivatives of methane; thus, isopentane is dimethyl-ethyl-methane, and neopentane is tetramethyl-methane.

In the case of hexane still another kind of iso-hydrocarbon is possible, in which there are two branches attached to different (inside) *C* atoms of the chain.

CHAPTER VIII.

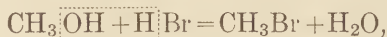
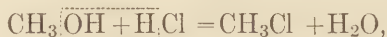
HALOGEN SUBSTITUTION PRODUCTS OF THE PARAFFINS.

If only one hydrogen atom of the hydrocarbon is replaced by a halogen atom the compound is called an **alkyl halide** (or **alkyl halogenide**), because it consists of a halogen atom linked to an alkyl radicle, e.g., $\text{CH}_3\text{—Cl}$ (see p. 86).

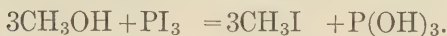
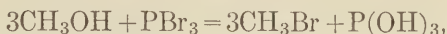
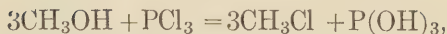
The **alkyl halides** derived from methane are methyl chloride or monochlormethane, CH_3Cl ; methyl bromide or monobrommethane, CH_3Br ; methyl iodide or moniodomethane, CH_3I .

General Methods of Preparation. (1) The chloride and bromide can be produced from methane by mixing chlorine or bromine with it and exposing the mixture to diffused sunlight

(2) All may be secured by acting on methyl alcohol with the proper halogen acid, in accordance with the following equations:



(3) Another method of obtaining them is by the action on methyl alcohol of PCl_3 , PBr_3 , and PI_3 :



In a manner exactly similar to the last two methods, the ethyl halides can be derived from ethyl alcohol.

Some of the More Important Alkyl Halides.

Methyl chloride (monochlormethane), CH_3Cl , is a gas under ordinary conditions. It is readily liquefied, the liquid boiling at -23.7° . It has been used as a local anæsthetic by spraying the liquid on to the skin from a strong glass container. The rapid evaporation causes the abstraction of enough heat from the skin to result in freezing the latter.

Ethyl chloride (monochlorethane), $\text{C}_2\text{H}_5\text{Cl}$, is a liquid boiling at 12.2° . It is put up in glass or metal tubes, and is used for local anæsthesia in the same way as methyl chloride. It is beginning to be used also as a general anæsthetic,¹ being administered as a vapour by inhalation.

Ethyl bromide (monobromethane), $\text{C}_2\text{H}_5\text{Br}$, is a liquid resembling chloroform in odour, density, and physiological effect. It boils at 38.37° (at 37.1° – 37.4° under 737 mm. pressure), and its specific gravity is 1.468 at 13° . It may be obtained by any of the general methods, but is best prepared by the action of ethyl sulphuric acid on potassium bromide, as in the experiment.

¹ In this book brief pharmacological statements are frequent. For full information on these points consult the excellent pharmacology text-books by *Cushny* and by *Sollmann*.

EXPERIMENT. Into a 250 c.c. flask put 55 c.c. of concentrated sulphuric acid; add quickly 55 c.c. of ethyl alcohol, shaking at the same time. Cool the flask by holding it in running water, add 38 c.c. of iced water, and cool again. Meanwhile set up a condenser having an adapter attached. Use a rapid stream of water in the condenser. Put into the flask 50 gm. of powdered

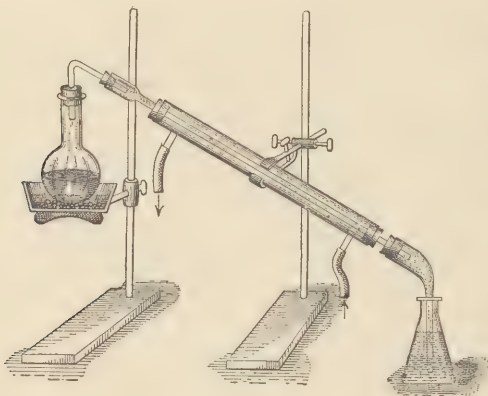


FIG. 19.

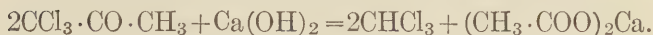
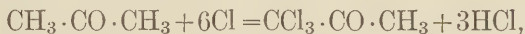
potassium bromide, then place the flask on a sand bath and attach to the condenser. Fill an Erlenmeyer flask one third full of ice-water and have the adapter dip below the surface of the water. Place this receiving flask in a bath of cold water. Heat rapidly and continue heating as long as any distillate comes over. Watch that the contents of the receiver be not sucked up into the condenser. If this is threatened turn the adapter so that air can enter it.

Decant most of the water from the ethyl bromide, then add ice-water and agitate. Decant the water. Wash several times in this manner. Finally shake the

stances. Chloroform is a very useful general anæsthetic, but is considered less safe than ether. Since it is not inflammable it can be used at night as an anæsthetic. It is not a stable compound, as exposure to light, air, and moisture causes some decomposition, thus furnishing the poisonous impurities, chlorine, hydrochloric acid, and carbon oxychloride or phosgene (COCl_2). These impurities can be readily detected, since chloroform containing them gives a precipitate when shaken with silver nitrate solution. Pure chloroform or other halogen substitution products do not immediately give a precipitate with silver nitrate, because they furnish no halogen ions (see p. 58). The addition of alcohol to chloroform, to the extent of one per cent, prevents decomposition. The method of its preparation is given in the following experiment. In it, chlorine (from bleaching-powder), chlorinates acetone, and from the product by the action of the calcium hydroxide present in the mixture chloroform is produced.

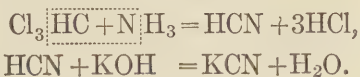
EXPERIMENTS. (1) *Preparation*. Into a litre flask put 500 c.c. of a saturated solution of calcium hypochlorite (prepared in advance for the class). Suspend a dropping funnel by the cork, also connect with a condenser. Into the funnel pour 20 c.c. of acetone and 40 c.c. of water, run this into the flask very slowly, shaking frequently. Heat the flask as long as droplets of chloroform appear with the water at the end of the condenser. Transfer the distillate to a separating funnel, shake with several *small* portions of water. Run the chloroform into a dry flask, add calcium

chloride, cork, and let it stand a day or so. As the yield is small, it need not be redistilled, but can be sealed up in sample bottles. The following equations will explain the reaction:



(2) To 1 c.c. of chloroform add half a test-tube of distilled water and shake vigorously. Remove the water with a pipette. Wash three times in this manner, testing the last wash-water with silver nitrate solution; if no precipitate appears, add silver nitrate to the washed chloroform. Let it stand, observing whether a precipitate forms later.

(3) Heat together in a test-tube 1 c.c. of chloroform, 5 c.c. of alcoholic solution of NH_3 ,¹ and 1 c.c. of alcoholic KOH .² Empty into an evaporating dish and evaporate not quite to dryness on a water bath. Note the odour of the residue. Dissolve the residue in a few cubic centimetres of water, and test for KCN by making strongly alkaline with NaOH , then adding a few drops of FeSO_4 solution and one drop of Fe_2Cl_6 solution. Boil two minutes, cool, acidify with HCl ; a greenish-blue colour should develop (see p. 4):



Bromoform (tribrommethane), CHBr_3 , is a liquid which boils at 146° at 751 mm. On cooling it becomes

¹ Made by bubbling NH_3 into alcohol.

² To 40 c.c. of alcohol add 20 c.c. of 30% KOH .

solid, melting at 9° . Its specific gravity is 2.885 at 15° . It has been used as a general anæsthetic, but is unsafe.

Iodoform (triiodomethane), CHI_3 , is a yellow crystalline solid, the crystals having the form of hexagonal plates. Its odour is peculiar and characteristic. It melts at 119° . Its specific gravity is 4.008. It is used in surgery as an antiseptic, the action being probably due to iodine which is freed. It is manufactured from acetone by the action of iodine and potassium carbonate. Its method of preparation is illustrated in the following experiment.

EXPERIMENTS. (1) Dissolve 5 gm. of sodium carbonate in 30 c.c. of warm water, add 5 c.c. of alcohol, heat in a water bath to $70\text{--}80^{\circ}$, add a little at a time 3 gm. of powdered iodine, shaking frequently. If the liquid has become brown, add just enough sodium carbonate solution to change it to a pale yellow. After cooling, filter and wash the crystals. When dried in a desiccator, a melting-point determination may be made.

The reactions involved are doubtless the production of iodal, $\text{CI}_3\cdot\text{CHO}$, by action of NaIO ; then the conversion of iodal by the action of the alkali present into iodoform and sodium formate.

(2) Make a yellow solution of iodoform in alcohol, set it aside loosely covered; by slow evaporation of the alcohol hexagonal crystals of considerable size are formed.

This reaction, besides being given by alcohol, is given by aldehyde, acetone, and other compounds which

contain the group $\text{CH}_3\cdot\text{CO}$ —, provided the CO is not part of a carboxyl group. (See p. 165.) On account of its strong odour, the production of iodoform in this manner is often used as a test for the presence of alcohol or other substances containing the above group.

Iodoform Substitutes. Because of the unpleasant odour of iodoform many antiseptic preparations have been put on the market which disguise or eliminate the bad odour. Such are *eka-iodoform* (iodoform with paraformaldehyde), *iodoformin* (iodoform with hexamethylenetetramine), *iodoformogen* (protein compound of iodoform), and *anozol* (iodoform and thymol). *Diiodoform* is tetraiodoethylene, C_2I_4 (see ethylene, p. 269).

Tetraiodomethane, CI_4 , is a solid, having a very high specific gravity, 4.32.

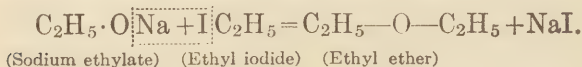
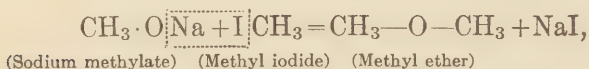
Similar to the alkyl halides are the alkyl combinations with metals, as zinc methyl, $\text{Zn}(\text{CH}_3)_2$, and sodium methyl, NaCH_3 . Both of these are important reagents.

CHAPTER IX.

ETHERS.

THE alkyl oxides are called ethers. They consist of two organic radicals linked to an oxygen atom, as methyl ether, $\text{CH}_3\text{—O—CH}_3$; ethyl ether, $\text{C}_2\text{H}_5\text{—O—C}_2\text{H}_5$.

A general method of *synthesis* is shown by the following equations:



Methyl ether is a gas and is unimportant.

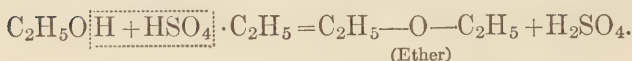
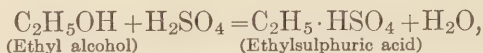
Ethyl ether is common ether. Pure ether is a liquid, boiling at 34.6° (33.6° at 734 mm. barometric pressure) and having a specific gravity of 0.718 at 15.6° and 0.7079 at $\frac{25^\circ}{4^\circ}$. It dissolves to a certain extent (about 6.5 per cent) in water; it also takes up about $1\frac{1}{4}$ per cent of water. Magnesium bromide removes both alcohol and water from ether when allowed to stand for some time. To obtain absolute ether, it is necessary to distil after the addition of metallic sodium to the ether ($\text{Na} + \text{H}_2\text{O} = \text{NaOH} + \text{H}$). It vaporizes readily, and, when rapidly evaporated, abstracts enough heat to freeze water if the latter is contained in a small

vessel surrounded by the ether. The vapour is heavier than air and consequently falls. It is very inflammable, and should therefore be kept away from a flame. Ether is a solvent for a great number of substances. It is extensively used as an anæsthetic, being quite safe when properly administered. Heat is liberated when chloroform and ether are mixed in certain proportions.

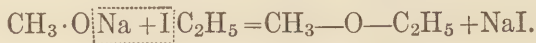
Because of the use of sulphuric acid in its production, it is sometimes called sulphuric ether. To prepare it, ethyl alcohol is allowed to slowly flow into heated ethylsulphuric acid (see p. 104) contained in a flask. The following experiment will make clear how this is done.

EXPERIMENT. In a litre flask mix 165 c.c. of C.P. H_2SO_4 with 210 c.c. of alcohol. Fit a cork, pierced with three holes, into the mouth of the flask. One hole is to admit the bent tube connecting with the condenser, another holds a thermometer, and the third is for a dropping funnel which contains ethyl alcohol. The bulb of the thermometer is immersed in the liquid. A better arrangement is to introduce alcohol into the ethyl sulphuric acid in the form of vapour. For this it is necessary to have an extra flask in which to boil alcohol, which is connected with a tube extending to the bottom of the ether generator flask. When all is ready, place the flask on a sand bath and connect with the condenser. Submerge the receiving flask in a cold bath and use an adapter (*cf.* ethyl bromide, p. 103). Heat rapidly until the ethylsulphuric acid has a temperature of 140° , at which point it must be kept for the rest of the process. Run

in a *very little* alcohol from the funnel, or vapour from the alcohol flask. At intervals, i.e., when the amount of ether vapor diminishes, add more alcohol, a few cubic centimetres at a time. Keep flames away from the vicinity of the receiving flask. Watch the apparatus constantly. When sufficient distillate has been secured, wash it with dilute NaOH solution in a separating funnel, then with several small portions of water; draw off the water, pour the ether into a dry flask, add calcium chloride, and cork tightly. Redistil after a day or so. The following equations will explain the reaction:



Mixed ethers contain two different organic radicles linked to the same oxygen atom, as methyl ethyl ether, $\text{CH}_3\text{—O—C}_2\text{H}_5$. They may be formed by a synthetic process similar to that described above for simple ethers, thus:



It is interesting to note that the boiling-point of methyl ethyl ether (11°) is intermediate between that of dimethyl ether, $(\text{CH}_3)_2\text{O}$ (-23.6°), and that of diethyl ether, $(\text{C}_2\text{H}_5)_2\text{O}$ (34.6°).

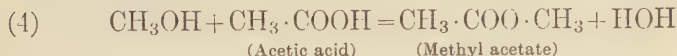
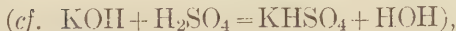
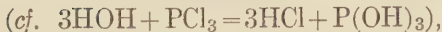
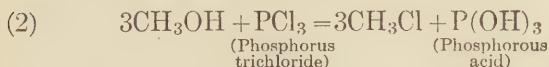
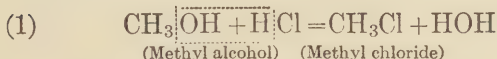
The ethers are very stable, not being affected by boiling with alkali or dilute acid.

CHAPTER X.

PRIMARY ALCOHOLS.

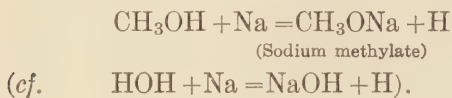
ONE of the most important classes of organic compounds are the alcohols. The empirical formula of a monacid alcohol can be derived from the formula of the paraffin hydrocarbon containing the same number of carbon atoms, by attaching an atom of oxygen, thus: $C_nH_{2n+2}O$.

Alcohols, however, are not oxides of the hydrocarbons. They are *hydroxides*. A primary alcohol is an *alkyl hydroxide*. Alcohols cannot be obtained by direct oxidation of the hydrocarbons. *That the oxygen atom is present in hydroxyl* is proven by the following reactions:

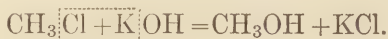


The striking similarity between the reactions of alcohol and the most typical of all hydroxides (viz., KOH and H_2O) is clearly shown by these reactions.

The reaction of potassium and sodium with alcohols shows further that one particular hydrogen atom of the latter has a different linking from that of the other three hydrogen atoms:



Finally, the structure of an alcohol is settled beyond a doubt by its *synthesis* from an alkyl halide by the action of a strong hydroxide:



Inorganic hydroxides are strong bases, because they furnish many hydroxyl ions when dissolved in water (see p. 149). Alcohols, on the other hand, *are not bases*; they ionize very slightly, if at all. It is to be noted that the change of one hydrogen atom of the hydrocarbon molecule into hydroxyl greatly alters the chemical behaviour of the compound; the paraffin is very stable and enters into reaction with very few reagents, whereas the alcohol is quite *reactive*, being readily affected by many reagents. The heat of combustion of an alcohol is less than that of the corresponding hydrocarbon. This is just what we should expect since there is oxygen in the alcohol molecule.

MONACID PRIMARY ALCOHOLS.

These comprise the most important group of alcohols. They form an homologous series beginning with methyl alcohol. There is a regular increase of specific gravity and boiling-point from the lowest to the highest members of the series.

Methyl alcohol (methanol, carbinol), $\text{H}\cdot\text{CH}_2\text{OH}$ or CH_3OH , is obtained from the distillate produced by the destructive distillation of wood (see p. 139). The crude alcohol is therefore called wood alcohol. It is also secured by destructive distillation of vinasse, which is the residue left after ordinary alcohol has been distilled off from fermented beet sugar molasses.

Fractional distillation does not suffice to free the methyl alcohol from the acetic acid, acetone, and other constituents of crude wood spirits.

A crystalline compound, methyl oxalate $(\text{CH}_3)_2\text{C}_2\text{O}_4$, can be formed by treatment with oxalic acid. The purified crystals can then be decomposed by boiling with ammonia water, yielding pure methyl alcohol:

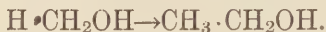


The process of production of pure methyl alcohol is more difficult and expensive than is that of ethyl alcohol.

Methyl alcohol boils at 64.5° , and its specific gravity at $\frac{15.6^\circ}{15.6^\circ}$ is 0.7931 (at $\frac{20^\circ}{4^\circ}$ it is 0.7913). Its melting-point is higher than that of ethyl alcohol, -93.9° . It mixes readily with water, exhibiting the phenomena of contraction of volume and liberation of heat. It

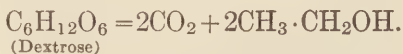
is a useful solvent; in consequence, the crude alcohol is used in the preparation of paints. It is intoxicating if taken internally; crude wood alcohol is dangerous, however, having caused many deaths when used as a substitute for ethyl alcohol. Wood alcohol burns with a blue flame, hence its use in alcohol lamps.

Ethyl alcohol (ethanol), $\text{CH}_3 \cdot \text{CH}_2\text{OH}$ or $\text{C}_2\text{H}_5\text{OH}$, is common alcohol. Its relation to methyl alcohol is seen when it is considered as methyl alcohol in which one hydrogen atom is replaced by the methyl radicle:



The name *methyl carbinol* expresses this relation. Similarly the higher alcohols are called carbinols (the prefix in each case indicating the groups attached).

Alcohol is produced by fermentation of dextrose (glucose) by means of yeast:



About five per cent of the dextrose forms by-products, such as amyl alcohol, glycerol (i.e., glycerine), and succinic acid. It has been thought that lactic acid is an intermediate product of yeast fermentation; and that this is converted into acetaldehyde and formic acid, the latter in turn giving up H (and evolving CO_2) which adds itself to the aldehyde molecule, and thus ethyl alcohol results. This theory has not been proven, and is rather discountenanced by the fact that yeast will not produce alcohol from lactic acid, nor from an equimolecular mixture of formic acid and acetaldehyde (even when these are set free in the reaction mixture).

Alcoholic beverages are obtained by fermentation of fruit juices containing sugar, as wine from grapes, or of malted grain, as beer from barley. Fermentation is inhibited when the alcohol content reaches about seventeen per cent. Malt liquors contain from two to eight per cent of alcohol. Wines contain eight to fifteen per cent. Stronger wines are made from these by adding alcohol. Brandy is obtained by distillation of wine, whiskey by distillation of fermented grain; both of these contain forty to sixty per cent of alcohol. Many liquors require ageing in order that the by-products which are disagreeable and injurious, as for instance fusel-oil, may be converted into ethereal compounds of pleasant taste and odour. The amount of alcohol present in a liquor can be readily estimated by distilling 100 c.c. of the liquor (diluted with 50 c.c. of water); when 100 c.c. of distillate has been collected, its specific gravity is determined. The percentage of alcohol is found by referring to tables of specific gravities (see Appendix, p. 403).

Preparation. Commercial alcohol is made from the cheapest forms of starch, potato or corn. The ground or mashed raw material is superheated ($140\text{--}150^\circ$) with steam under pressure; then the pressure is suddenly lowered, causing the moisture within the starch granules to turn into steam and thus to rupture the granules by the explosive effect. After cooling, malt¹ is added and the mixture is kept at $60^\circ\text{--}62^\circ$. Malt contains a ferment, *diastase*, which changes starch

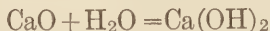
¹ Malt is obtained by allowing barley to germinate to a certain stage.

into the sugar maltose, and, to the extent of about 20 per cent, into dextrin. The sugar solution is diluted, and yeast is added.

The yeast furnishes a ferment which splits or inverts the maltose molecule into two dextrose molecules, and also a ferment which decomposes the dextrose into alcohol and carbon dioxide. These ferments can be extracted from the yeast cells by grinding the latter with fine quartz sand and subjecting the mass to a very high pressure (up to 300 atmospheres), and finally filtering the extract through porcelain. This filtrate contains no yeast cells, but it inverts maltose into dextrose and changes dextrose into alcohol.

The ferment in this cellular extract from yeast is called *zymase*. Similar intracellular ferments can be obtained from certain bacteria. Ferments are often called *enzymes*.

The weak alcoholic solution (not over 18 per cent) is next subjected to distillation, using a fractionating column. The crude distillate (90 per cent alcohol) is filtered through animal charcoal, which removes many impurities. It is then redistilled, the product being *ordinary alcohol* (95 per cent). This is apt to contain some aldehyde. The strongest alcohol obtainable by the most careful fractionation contains 4.5 per cent by weight of water. Commercial absolute alcohol contains about one half of one per cent of water. It is obtained by digesting alcohol with quick-lime and then distilling.



More nearly absolute alcohol is secured by treating with metallic sodium and distilling. In this country corn starch is mostly used for alcohol production, 2.7 gallons can be secured from one bushel of corn. In Europe potatoes are used. The cost of the *process* of manufacture is said to be very low, less than five cents per gallon.

Properties. *Chemically absolute alcohol* is almost unknown, because it takes up moisture so rapidly when exposed to the air. Absolute alcohol has a specific gravity of 0.79388 at $\frac{15.56^\circ}{15.56^\circ}$, 0.79357 at $\frac{15^\circ}{4^\circ}$, and boils at 78.3° (corrected) (at 734 mm. pressure it boils at 77.7°). It solidifies at -112° . It has much less odour than common alcohol. Alcohol containing 95.57 per cent by weight has the lowest boiling-point of any alcohol preparation, 78.15° at 760 mm. Alcohol burns with a colourless flame. When mixed with water, rise of temperature and contraction of volume are observed. It is an intoxicant; the detrimental effect of alcoholic liquors, however, is due *in part* to other compounds besides the alcohol. Alcohol is of great service as a solvent. *Methylated* or *denatured* alcohol is alcohol to which wood alcohol or nauseous substances have been added to render it unfit to drink. In the United States 10 parts of wood alcohol and 0.5 part of benzine, or else 2 parts of wood alcohol and 0.5 part of crude pyridine per 100 parts of alcohol, are used. Such alcohol can be sold duty-free in many countries.

EXPERIMENT. Into a large bottle or flask put 500 c.c. of 10% glucose solution, and add some crumbled

yeast. Through a cork, which tightly fits the bottle or flask, pass a glass tube which is bent so as to extend down into a small bottle containing some baryta water, the tip of the tube just reaching the surface of the latter; through a second hole in its cork the baryta bottle is connected with a tube or tower of soda-lime. Thus CO_2 cannot enter the apparatus from without. Let it stand a few days, after which a copious precipitate of BaCO_3 is obtained.

Experiments with 95% alcohol. (1) Shake 10 c.c. in a test-tube with anhydrous CuSO_4 and let it stand (corked) one hour; the CuSO_4 becomes bluish (with absolute alcohol no blue colour appears). Explain what takes place.

(2) Take 52 c.c. of alcohol and 48 c.c. of water, each being at a temperature of 20° , mix them in a 100 c.c. graduate, note the maximum temperature, cool to 20° , and read off the volume (about 96.3 c.c. instead of 100 c.c.).

When miscible liquids are mixed a change in volume is generally noticed, usually a decrease (sometimes an increase). Heat may be either absorbed or given off.

(3) Put 10 c.c. of alcohol in a test-tube, add as a bottom layer 5 c.c. of concentrated sulphuric acid. Throw in a number of small crystals of potassium permanganate. Flashes of fire will occur in the liquid in the zone of contact of the alcohol and acid (ozone production, and intense oxidation of a derivative of alcohol).

Of other primary alcohols little need be said here.

Propyl alcohol is $\text{CH}_3 \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{OH}$.

Normal butyl alcohol is $\text{CH}_3 \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{CH}_2\text{OH}$.

Primary isobutyl alcohol is $\text{CH}_3 \cdot \text{CH} \cdot \text{CH}_2\text{OH}$.



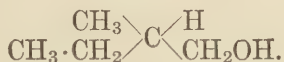
As with hydrocarbons the branching of the chain lowers the boiling-point.

Normal amyl alcohol is $\text{CH}_3 \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{CH}_2\text{OH}$.

Primary isoamyl alcohol, called isobutyl carbinol, is $\text{CH}_3 \cdot \text{CH} \cdot \text{CH}_2 \cdot \text{CH}_2\text{OH}$; this is the main constituent



of *fermentation amyl alcohol*. Both of these amyl alcohols are contained in fusel-oil and in certain liquors, especially recently, distilled brandy and whiskey. They are poisonous. There are three isoamyl alcohols having the same structural formula,



Their chemical and physical properties are identical, except that their action on polarized light is different. One rotates the beam of light to the left, another rotates it to the right—these are the *active amyl alcohols*; the third does not cause rotation and is called *inactive amyl alcohol*.¹ There is also another amyl alcohol containing the primary alcohol group,



¹ For a discussion of this form of isomerism, see p. 199.

There are four secondary amyl alcohols, two normal and two isoamyl alcohols.

There is a **tertiary isoamyl alcohol**,



which has been used as a hypnotic under the name **amylene hydrate**.

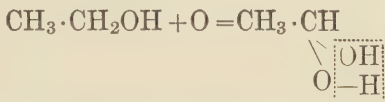
CHAPTER XI.

ALDEHYDES.

If a primary alcohol be oxidized the first product is an aldehyde:



Two atoms of hydrogen have been removed from the alcohol molecule, hence the name *al(cohol) dehyd(ro-genatus)*. The reaction is more accurately indicated as follows:



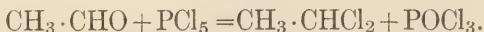
Two hydroxyls become attached to the same carbon atom, but, as is the rule¹ in organic compounds, such a combination is too unstable to persist and H_2O splits off.

It is to be noticed that the *aldehyde group* $-\text{CHO}$ contains no hydroxyl. This can be proven experimentally. If alcohol or any other hydroxyl-containing compound be treated with phosphorus pentachloride, the place of each hydroxyl group is taken by one chlorine atom:



¹ There are three well-known exceptions to this rule, in the case of chloral hydrate, mesoxalic and glyoxylic acid.

But if an aldehyde be similarly treated a dichlor-compound is obtained:

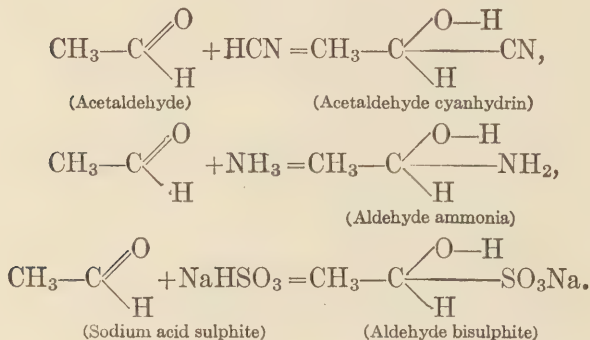


Therefore the aldehyde group must be written CHO, not COH. Nascent hydrogen converts an aldehyde into the corresponding primary alcohol.

The aldehydes are named from the acids which they produce when oxidized: thus, $\text{H} \cdot \text{CHO}$ is formic aldehyde or formaldehyde, and $\text{CH}_3 \cdot \text{CHO}$ is acetic aldehyde or acetaldehyde.

Aldehyde reactions. (1) All aldehydes are strong reducing agents, because they readily take up oxygen to form acids. The common tests for sugar are really aldehyde reactions, as practically all sugars contain the CHO group. The reduction of silver and copper salts is illustrated by the experiment below.

(2) The linking $\text{C}=\text{O}$ in the aldehyde group causes aldehydes to act like unsaturated compounds, for they readily form addition compounds, thus:

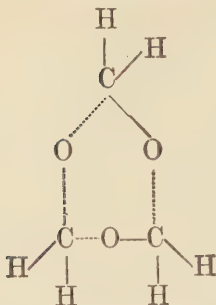


(3) Phenylhydrazine can combine with an aldehyde by removing O of the carbonyl group, forming a *hydrazone*.

(4) Aldehydes (except chloral hydrate) cause a violet-red colour to appear when added to a solution of fuchsin which has been decolorized by sulphurous acid. This reaction is due to the formation of condensation products (see acetaldehyde). Dextrose does not give this test because, as in the case of chloral hydrate, it does not contain a $C=O$ group; however, in the case of both of these compounds the aldehyde character appears under the influence of the strong reagents (and the heat) used for other tests.

Formaldehyde (methanal), $H \cdot CHO$, is a gas. It is quite soluble in water. Commercial *formalin* is a 40 per cent solution. Formaldehyde may be prepared by bubbling air through methyl alcohol which is kept at about 50° ; then the mixture of air and vapour is passed through a heated tube containing a copper or platinum spiral: $H \cdot CH_2OH + O = H \cdot CHO + H_2O$. It is also produced by burning methyl alcohol in a special lamp in which the supply of air is limited, so that incomplete combustion occurs; part of the alcohol is oxidized to formaldehyde and escapes. This lamp can be used for disinfection of rooms.

Formaldehyde has a tendency to form *polymers*. A polymer has a molecular weight which is an even multiple of that of the original substance, and it has the same percentage composition as the latter. Thus **paraformaldehyde** is $(H \cdot CHO)_n$. Some think that n has a value of 3, and it is definitely stated to be not less than 3. The graphic representation of $(H \cdot CHO)_3$ would be



Paraformaldehyde (paraform) is a white substance, which, on being heated, is converted into formaldehyde. It is sold in the form of tablets or candles for disinfecting purposes.

With ammonia formaldehyde does not form a simple addition compound as do other aldehydes, but a complex substance, hexamethylenetetramine (see p. 192).

Formaldehyde is an efficient germicide, and is therefore used extensively for disinfecting purposes. It is used either as the gas or in dilute solution. It is very irritating to the eyes and mucous membranes. The dilute solution also hardens albuminous substances, and is consequently used to prepare tissues for histological examination. It converts a solution of gelatin into a hard insoluble mass.

Glutol is a substance produced by the action of formaldehyde on gelatin, as a dry powder it is used as a surgical dressing for raw surfaces. It is said to act as an antiseptic because of slow liberation of formaldehyde.

EXPERIMENTS. (1) To a few cubic centimetres of concentrated H_2SO_4 in a test-tube add a few drops of ferric chloride solution; with a pipette run in about

5 c.c. of milk containing formaldehyde solution as a top layer, avoiding mixing with the H_2SO_4 —a violet zone between the two layers forms, quickly disappearing.

(2) Set in a desiccator an evaporating dish containing 5 c.c. of formalin. Leave several days until a white solid, paraformaldehyde, is obtained. When this is secured, heat some of it in a dry test-tube. It volatilizes completely, passing away as formaldehyde gas. Note the odour. Be careful not to get strong fumes into the eyes or nostrils, as the gas is very irritating.

(3) To 10 c.c. of milk in a large evaporating dish add a little formaldehyde and 10 c.c. of concentrated hydrochloric acid containing one drop of 5% ferric chloride. Heat over the flame, holding the dish in the hand and maintaining a rotary motion. At about 90° the mixture acquires a violet colour.

(4) In a large evaporating dish put 60 c.c. of milk to which a little formaldehyde has been added. Float on the milk a watch-glass containing about 1 c.c. of a fresh solution of 0.35% of morphine sulphate in C.P. H_2SO_4 . Cover the evaporating dish with a glass plate. Note the time it takes to secure a purple margin or general colouration of the acid. The acid solution of morphine must be kept away from formaldehyde vapours and the solution should be freshly prepared.

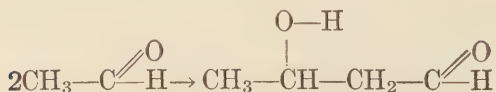
(5) Add 4 drops of methyl alcohol to 3 c.c. of water in a test-tube. Make a spiral of copper wire which will easily slip into the tube. Heat the wire until red hot and plunge it into the solution. Repeat this several times. Cool the liquid, add 1 drop of 0.5% resorcinol solution, and with a pipette run in a bottom layer of 5 c.c. of concentrated sulphuric acid. A red

zone develops. Why is formaldehyde produced by this procedure? This is used as a test for small quantities of methyl alcohol.

Acetaldehyde (ethanal, aldehyde), $\text{CH}_3 \cdot \text{CHO}$, can be obtained in similar manner as formaldehyde by the oxidation of ethyl alcohol vapour, induced by heated platinum. The oxidation is generally effected, however, by the use of sulphuric acid and sodium or potassium dichromate as described in the experiment below. Acetaldehyde boils at 20.8° and has a specific gravity of 0.780 at 20° .

Acetaldehyde can be changed into the polymers, **paraldehyde**, a liquid boiling at 124° , and **metaldehyde**, a solid. Both have the formula $(\text{CH}_3 \cdot \text{CHO})_3$. It is supposed that the difference in their structural formulæ is a stereomeric difference (see p. 199), that is, a difference in the arrangement in space of a CH_3 group in relation to the rest of the molecule. Paraldehyde is a hypnotic.

Aldehyde molecules can be made to fuse together, forming a "condensation" product, *aldol*. Zinc chloride will effect this change:



It has been suggested that the production of starch and sugar by plants is due to condensation and polymerization of formaldehyde, the latter being synthesized from CO_2 and H_2O . A sugar can be made from formaldehyde by condensation under the influence of lime-water (see p. 247).

EXPERIMENTS. *Preparation.* (1) Mix in a large flask 100 c.c. of water and 30 c.c. of C.P. H_2SO_4 . Fit a cork having two holes, one for the bent tube connecting with a condenser, the other for a dropping funnel. Have the

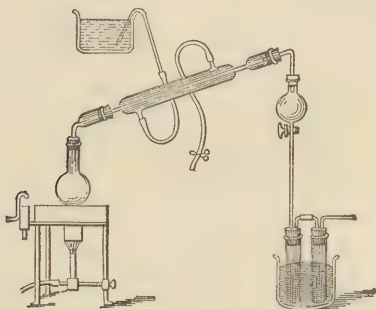
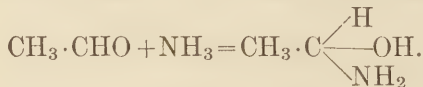
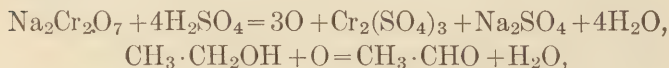


FIG. 20.

tip of the dropping funnel about 3 cm. above the liquid. Connect with the condenser, and place the receiving flask in ice-water. Heat the flask over wire gauze to the boiling-point. Now add through the funnel, in a slow stream, a solution of sodium dichromate (100 gm. of dichromate dissolved in 100 c.c. of water, and mixed with 53 c.c. of alcohol). Remove the flame as soon as distillation is well started. If vapour passes through uncondensed, slacken the stream. If aldehyde ceases distilling, heat again with the flame. When all of the solution has been added, redistil the distillate. Save a portion of the crude distillate for making the aldehyde tests given below. In redistilling tilt the condenser upward, as shown in the diagram. Circulate through it water heated to 30° , using a reservoir or large funnel. Connect the condenser with a dropping

funnel, which dips into the ether in the first wash-bottle. Put 25 c.c. of dry ether into each wash-bottle. The aldehyde will not condense at 30°, while alcohol and water will, so that only aldehyde passes into the ether, which absorbs it. Keep the ether bottles in a bath of ice-water. When the aldehyde seems to have all passed over, transfer the ether to a beaker which is placed in a freezing-mixture. Now bubble into it ammonia (secured by heating NH_4OH in a flask), which has been dried by passing through a tower of soda-lime, until the odour of ammonia becomes strong. A mass of white crystals of aldehyde ammonia will appear. Filter, wash the crystals with ether, and dry in a CaCl_2 desiccator. From this product pure aldehyde may be obtained by dissolving some of it in an equal weight of water, adding $3\frac{1}{2}$ times as much 50% H_2SO_4 , and then distilling. Put some of the crystals in a sample bottle, hold the bottle obliquely, bottom up, and fill with ammonia gas, cork and seal with sealing wax.



(2) *Aldehyde tests.* (a) Add a little of the crude distillate to 5 c.c. of dilute Fehling's solution in a test-tube; boil until Cu_2O is precipitated.

(b) Add another small portion to a few cubic centimetres of ammoniacal AgNO_3 solution in a perfectly clean test-tube; heat gradually—a mirror of silver is deposited.

(c) To 1 c.c. of dilute rosaniline (fuchsin) solution add a solution of sulphurous acid until almost decolorized. Add some aldehyde solution and shake—a violet-red colour appears. Schiff's reagent is very convenient to use for this test.¹

Chloral (trichloraldehyde), $\text{CCl}_3 \cdot \text{CHO}$, is a chlorine derivative of acetaldehyde. It is produced by passing dried chlorine gas into absolute alcohol for several days. Aldehyde and HCl are the first products of the chlorination. The final products are chiefly chloral hydrate and chloral alcoholate, $\text{CCl}_3 \cdot \text{CH} \begin{smallmatrix} \text{OH} \\ \diagup \quad \diagdown \\ \text{OH} \end{smallmatrix}$ and $\text{CCl}_3 \cdot \text{CH} \begin{smallmatrix} \text{OC}_2\text{H}_5 \\ \diagup \quad \diagdown \\ \text{OH} \end{smallmatrix}$ respectively. Chloral is liberated from these by the action of concentrated sulphuric acid.

Chloral is an oily liquid, boiling at 97.7° and having a specific gravity of 1.512 at 20° . It gives the aldehyde reactions. When it comes into contact with water it forms chloral hydrate crystals.

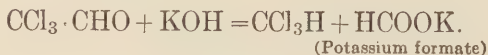
Chloral hydrate, $\text{CCl}_3 \cdot \text{C} \begin{smallmatrix} \text{H} \\ \diagup \quad \diagdown \\ \text{OH} \quad \text{OH} \end{smallmatrix}$, is believed to have two

hydroxyls attached to the same carbon atom, contrary to the general rule. It may be considered an addition compound of the aldehyde with water. One reason for believing that a typical CHO group is not contained in it is the fact that it does not give the fuchsin test.

Chloral hydrate is extremely valuable as a medicine,

¹ Prepare the reagent by saturating with SO_2 gas a solution of 2.2 gm. of rosaniline in 10 c.c. of water. Cork tightly and let it stand until light yellow or colourless. Dilute with 200 c.c. of water and keep in a dark-coloured bottle well stoppered.

being used as a hypnotic. It is very soluble in water and in alcohol. It melts at 57°. Alkaline solutions decompose both chloral and chloral hydrate to chloroform and formic acid:



EXPERIMENTS. (1) Try the aldehyde tests (see acetaldehyde) with a solution of chloral hydrate.

(2) Warm a few cubic centimetres of chloral hydrate solution; after adding NaOH, notice the odour of chloroform.

(3) Boil a few cubic centimetres of chloral hydrate solution; test part of it with AgNO_3 —it gives no precipitate. Now add some zinc powder to the original solution and boil two minutes. Filter; test filtrate with AgNO_3 —it gives a white precipitate of AgCl . The zinc decomposes water; the nascent hydrogen produced takes chlorine from the chloral hydrate, forming HCl (which combines with the zinc).

(4) To 2 gm. of chloral hydrate in a dry test-tube add 5 c.c. of C.P. H_2SO_4 , warm gently while shaking. An oily liquid (chloral) separates as a top layer. Cool the tube to room temperature, add 5 c.c. of chloroform which is free of alcohol and water. Draw off the top layer with a dry pipette, and allow the chloroform to evaporate, the residue in the dish will take up moisture from the air, resulting finally in the formation of chloral hydrate crystals.

Chloral Substitutes. Many derivatives of chloral have been synthetized with the object of correcting the

tendency which chloral hydrate has to depress the circulation. Such are:

Butyl-chloral hydrate (croton chloral),



Chloralamide, $\text{CCl}_3 \cdot \text{CH} \begin{smallmatrix} \text{OH} \\ \diagdown \\ \text{NH}_2 \end{smallmatrix}$

Chloralformamide, $\text{CCl}_3 \cdot \text{CH} \begin{smallmatrix} \text{OH} \\ \diagdown \\ \text{CO} \cdot \text{NH}_2 \end{smallmatrix}$.

Chloralose (chloral + glucose), $\text{C}_8\text{H}_{11}\text{Cl}_3\text{O}_6$.

Hypnal (chloral + antipyrin). :

Dormiol (chloral condensed with amylene hydrate).

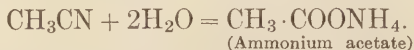
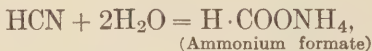
CHAPTER XII.

FATTY ACIDS AND ETHEREAL SALTS. FURTHER OBSERVATIONS IN PHYSICAL CHEMISTRY.

ACIDS.

ACIDS are defined as substances which when dissolved in water dissociate in such a way as to furnish hydrogen ions (see p. 58). Most organic acids dissociate but feebly; they are therefore weak acids as compared with inorganic acids (see p. 148). The majority of organic acids contain the carboxyl group.

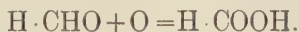
A general method of production of carboxylic acids is by *hydrolysis*¹ of a cyanide (see experiment under acetic acid):



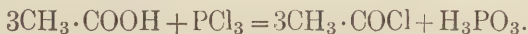
The acids to be studied at this point are called **fatty acids**, because common fats contain some members of this series of acids (in combination with glycerol). They are monobasic, i.e., they contain only one displaceable hydrogen atom in the acid group. They

¹ Hydrolysis means introducing H_2O into the molecule of the substance to be hydrolyzed, resulting in a product quite different from the original substance.

conform to the general formula, $C_nH_{2n}O_2$. They are the end products of the oxidation of primary alcohols, of the methyl alcohol series, since they can be obtained by oxidation of aldehydes:



The OH of carboxyl can be proven to be hydroxyl by the reaction with PCl_3 (see pp. 112 and 122), thus:



It would be desirable to call this series of acids the *formic acid series*, since the term fatty is misleading.

The boiling-points of these acids increase steadily with increase in the number of carbon atoms. For some unexplained reason a similar statement is not true of the melting-points, but on the contrary the acids having an odd number of carbon atoms have each a lower melting-point than the next acid having one less carbon atom.

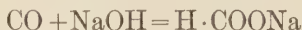
Formic acid (methanoic acid), $H \cdot COOH$, is a liquid.

(1) It can be made by oxidation of formaldehyde by hydrogen peroxide in alkaline solution (see exp.):



The acid can then be liberated from the potassium formate.

(2) Moist CO is absorbed by soda-lime at 190°–220°, forming sodium formate:



(3) Moist CO₂ coming in contact with metallic potassium forms potassium formate and potassium bicarbonate:



(4) Oxalic acid when heated with glycerol (glycerine) decomposes to formic acid and carbon dioxide (see exp.).

Formic acid occurs in red ants, in stinging nettles, and in the stinging apparatus of bees. It is very irritant, causing blisters when applied to the skin. Formic acid boils at 101°; it solidifies at a low temperature and melts at 8.3°. Its specific gravity is 1.2187 at 20°. It is a strong reducing agent, reducing silver and mercury compounds to the metal (see exp.). The full structural formula, $\text{H}-\overset{\text{O}}{\underset{\text{O}-\text{H}}{\text{C}}}=\text{O}$, shows that it

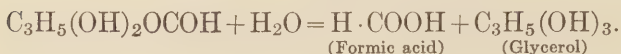
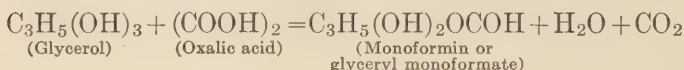
contains the aldehyde group overlapping the acid group, carbonyl being common to both. It oxidizes to carbon dioxide and water. It is a stronger acid than acetic acid. When treated with concentrated sulphuric acid it is decomposed, with evolution of carbon monoxide (see exp.).

EXPERIMENTS. (1) To 0.5 c.c. of commercial formaline in a beaker add 10 c.c. of 8% NaOH (twice

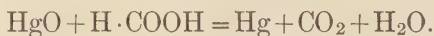
normal solution). Add hydrogen peroxide as long as effervescence continues and let it stand until no odour of formaldehyde remains. Titrate the solution with $\frac{N}{1}$ H_2SO_4 in the following manner: After putting a drop of methyl orange into the solution, run in the acid from a burette gradually, until the mixture remains slightly pink after stirring well. Deduct the number of cubic centimetres of H_2SO_4 from 20 c.c. (which would be neutralized by 10 c.c. of 8% NaOH); the difference indicates the amount of formic acid which has been produced. This method can be used for quantitative estimation of formaldehyde.

(2) Prepare formic acid also as follows: Into a half-litre flask put 50 c.c. of anhydrous glycerol (which has been heated at 170° for an hour); add 50 gm. of crystallized oxalic acid. Suspend a thermometer in the cork, so that its bulb is in the liquid. Heat gradually on a sand bath. Connect with a condenser. Carbon dioxide is evolved and formic acid begins to distil at about 115° (temperature of the liquid). When the temperature reaches 150° , cool the mixture to about 50° , then add 50 gm. of oxalic acid. Heat again up to 150° . If the mixture is overheated acrolein (p. 271) will be produced, which is a very disagreeable gas. Test some of the acid distillate for formic acid as below. If less than 200 c.c. of distillate is obtained, dilute it. In the meantime copper hydroxide has been prepared by treating $CuSO_4$ solution with KOH until slightly alkaline, diluting and filtering. In similar manner, prepare lead hydroxide from lead nitrate solution. Add to half of the formic acid copper hydroxide, warm-

ing the mixture. When copper hydroxide no longer dissolves, filter and set away for slow evaporation. To the rest of the acid add lead hydroxide and proceed as with the copper formate.



(3) Test for formic acid in the distillate as follows: Warm a few c.c. to 50°, add HgO, and shake vigorously. Filter and boil the filtrate one minute; a gray precipitate of mercury develops:



(4) Into a test-tube put 3 c.c. of undiluted formic acid; add slowly 6 c.c. of H₂SO₄. Cork quickly with a cork through which passes a bent delivery-tube the end of which is to dip into a few cubic centimetres of dilute hæmoglobin solution in another test-tube. The hæmoglobin is changed to carbon-monoxide-hæmoglobin, which has a cherry-red tint. The hæmoglobin solution is made by adding a drop of blood to a little distilled water.

Acetic acid, CH₃COOH. There are various ways by which ethyl alcohol may be oxidized to yield acetic acid. In the laboratory, the addition of spongy platinum to alcohol contained in an open vessel causes the atmospheric oxygen to attack the alcohol, oxi-

dizing it and producing acetic acid. The spongy platinum itself undergoes no change; it is a *catalytic* agent, merely transferring the oxygen to the alcohol.

Pure alcohol or alcohol diluted with pure water does not spontaneously become converted into acetic acid when exposed to the air, but does so if the dilute alcoholic solution contains nitrogenous matter. This is because of the growth in the latter solution of a microörganism derived from the air (*Mycoderma aceti*), which, like spongy platinum, transfers atmospheric oxygen to the alcohol. Nitrogenous matter is necessary for the life of this organism. It is in this way that wine becomes converted into vinegar. Mere exposure of wine or cider to air would, however, occupy too much time to produce sufficient vinegar to meet the demands of commerce, and consequently the above process has to be accelerated. This is done by allowing the wine to slowly percolate through freely perforated barrels filled with beech shavings previously sown with the mycoderma by soaking them in strong vinegar. A slight amount of heat is generated during the oxidation; this creates currents of air which enter the barrels through the perforations in their sides, and in this way a sufficiency of oxygen for the process is supplied. Other alcoholic solutions besides wine may be used for the purpose, e.g., cider or beer, and frequently some alcohol obtained by fermenting glucose is added to these. The amount of alcohol in such solutions should not, however, be over ten per cent. The resulting vinegars contain about five per cent of acetic acid, besides various aromatic bodies.

To obtain acetic acid in a pure state, fermentation

of alcoholic liquids is, however, not employed. For this purpose wood is subjected to what is known as *destructive distillation*. It is heated at low temperature (200°) in an iron retort from which air is excluded, and the vapours condensed. The resulting distillate consists of a mixture of a tarry material and a watery liquid known as pyroligneous acid. This latter contains, besides acetic acid (10%), various other organic substances, particularly acetone (0.5%) and methyl alcohol (1—2%). By fractional distillation several of these are separated, the second fraction, which contains most of the acetic acid, being neutralized with quicklime and evaporated; the resulting calcium acetate is then freed of impurities by heating and treated with hydrochloric acid so as to liberate the acetic acid, which is then distilled. This first distillate contains about 36 per cent of acetic acid. To further purify it, this dilute acid is passed through charcoal, and then redistilled over potassium dichromate. The final distillate, however, still contains water. To separate this, the solution is cooled down to a low temperature, when most of the acid solidifies and the water can be drained off. Since pure acetic acid solidifies on cooling, it is often called *glacial acetic acid*.

Acetic acid is a colourless liquid, boiling at 118.1° (corrected) and with a specific gravity of 1.055 at 15° . By dilution with water the specific gravity rises, attaining the maximum when an acid of 80% is obtained (see table in Appendix, p. 408). When glacial acetic acid is cooled it solidifies, the crystals again melting at 16.6° . It has a characteristic odour and, in dilute solution, a pleasant acid taste.

EXPERIMENTS. (1) Into a small fractionating flask put 6 gm. of potassium dichromate and 10 c.c. of concentrated H_2SO_4 ; connect with a condenser; then, by means of a dropping funnel suspended by the cork of the flask, add drop by drop 12 c.c. of 20% alcohol. Heat until enough distillate is secured for the following tests.

(2) *Acetic acid tests.* (a) To 5 c.c. of the solution add 1 c.c. of H_2SO_4 and a few drops of alcohol. Shake, and note the odour of ethyl acetate on warming.

(b) Neutralize 5 c.c. with sodium carbonate solution. When neutral add a few drops of ferric chloride solution. The mixture becomes brownish red; on boiling a coloured precipitate separates out. Filter; the filtrate is colourless.

(3) Cool some glacial acetic acid in a large test-tube by means of ice-water, stirring with a thermometer. Melt the crystals with the heat of the hand, keeping the thermometer in motion, note the temperature at which the acid melts.

In all its reactions acetic acid conforms with the structural formula CH_3COOH . Since, in our practical exercises, we shall perform nearly all the reactions which have enabled chemists to ascribe this formula to acetic acid, it may be advantageous, when describing these reactions, to indicate how they bear out the structural formula. To illustrate clearly just exactly *how a structural formula is arrived at* by the chemist let us suppose that we are working with an unknown substance which, by elementary analysis and molecular weight determination (see Chapter III and p. 75),

we have found to possess the empirical formula $C_2H_4O_2$.

For the sake of clearness of comprehension of the steps of the argument for the structural formula, a tabulated statement will be given before the detailed discussion.

(1) $C_2H_3O_2-H$, proof: monobasic acid.

(2) C_2H_3O-OH , proof: phosphorus chloride reaction.

(3) $CH_3-(OC)-OH$, methyl group proven by production of CH_4 from an acetate.

(4) $CH_3-COO-H$, proof: the addition of CO_2 to CH_3Na forming an acetate.

(5) *Synthetically* by the building up of methyl cyanide from CH_4 , and the hydrolysis of the cyanide to acetic acid.

(1) In testing the reaction of this substance we shall have found it acid, and on neutralizing it with monacid bases and evaporating, crystalline salts will be obtained which on analysis will be found to contain one H atom less than the acid itself. These facts indicate that the acid dissociates into a cation of hydrogen, H^+ , and an anion represented by the remainder of the molecule, $C_2H_3O_2'$. In other words, one of the four H atoms must be represented in the structural formula as different from the others: $C_2H_3O_2-H$.

The hydroxides which may be employed to neutralize

the acid are conveniently divided into metallic and organic.

Metallic salts of acetic acid—the acetates—are very numerous. *Sodium and potassium acetates* ($\text{C}_2\text{H}_3\text{O}_2\text{K}$; $\text{C}_2\text{H}_3\text{O}_2\text{Na}$) are extensively used for various purposes in the laboratory. *Lead acetate*, $\text{Pb}(\text{C}_2\text{H}_3\text{O}_2)_2$, on account of its possessing a peculiar sweetish taste, is known as sugar of lead. It is used in medicine as an astringent. When it is mixed with lead oxide the

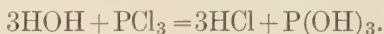
compound is known as *basic lead acetate*, $\text{Pb} \begin{array}{l} \text{OH} \\ \diagdown \\ \text{C}_2\text{H}_3\text{O}_2 \end{array}$.

In the presence of carbonic acid, basic lead acetate forms densely opalescent solutions on account of the insoluble lead carbonate which is formed. In boiled distilled water the solutions are nearly clear. The lead acetates are valuable precipitating reagents and are extensively employed for this purpose in bio-chemistry. *Copper acetate* is a well-known salt and is used as a reagent. All these acetates are most simply prepared by dissolving the metallic hydroxides in acetic acid.

Ethereal Salts of Acetic Acid. In studying alcohol we saw that its hydroxyl group (OH) is replaceable, for example, by halogens (Cl, Br, or I), or, as in the case of ethereal salts, by the organic acid radicle $\text{C}_2\text{H}_3\text{O}_2$. Since the ethereal salts are of considerable importance and are numerous, we shall postpone their consideration till later.

(2) So far we have seen that one of the H atoms in acetic acid differs considerably from the others. By another set of reactions we can show that this same H atom must be intimately connected with one of the O atoms, the resulting group, which we have already

met with in alcohols, being hydroxyl. This hydroxyl is, as we have seen, replaceable by halogens. Thus, when acetic acid is treated with PCl_3 , the following reaction ensues: $3\text{C}_2\text{H}_3\text{O}_2\text{H} + \text{PCl}_3 = 3\text{C}_2\text{H}_3\text{OCl} + \text{H}_3\text{PO}_3$. The hydroxyl group is evidently substituted by Cl, just as in the case of water or alcohol:



We must therefore assume that acetic acid can under certain conditions be caused to split up into $\text{C}_2\text{H}_3\text{O}$ and OH . The former of these is called the *acetyl group*, the latter is of course hydroxyl.

Acetyl chloride, $\text{C}_2\text{H}_3\text{OCl}$, belongs to the class of *acid chlorides* (or acyl halogenides) and may be prepared by the method described in the following experiment:

EXPERIMENT. Put 25 c.c. of glacial acetic acid into a fractionating flask. Suspend a dropping funnel by the cork. Attach the flask to a condenser. As a receiver, fit a filtering flask on to the condenser-tube with a cork (see fig. 21), and attach to the side tube of the filtering flask a calcium chloride tube. All moisture must be carefully excluded in this manner. Add to the acid through the dropping funnel 20 gm. of phosphorus trichloride, the flask being immersed in a bath of ice-water. When cooled, substitute a warm bath at 40° – 50° . Keep the temperature at this point until the evolution of HCl ceases (have the apparatus under a hood). Bring the water of the bath to active boiling and distil the acetyl chloride.

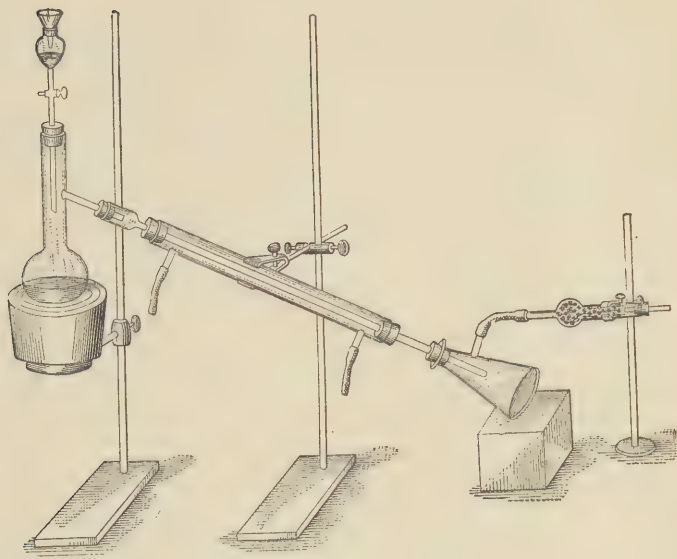
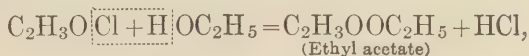


FIG. 21.

It is a colourless volatile fluid, boiling at 51° . In the presence of water it readily decomposes, as represented in the following equation:



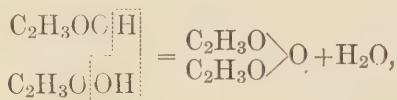
The atmospheric moisture is sufficient to cause this reaction, so that when acetyl chloride is exposed to the air it fumes, the fumes being very suffocating and disagreeable. (It should be kept in tightly stoppered bottles.) The H of the hydroxyl group of alcohols reacts similarly with acetyl chloride, thus:



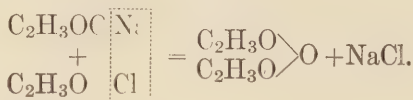
the ethereal salt of acetic acid with the radicle of the alcohol used being formed. On this account acetyl chloride is an invaluable reagent for the detection of alcoholic hydroxyl; if we find that a substance when treated with acetyl chloride forms an ethereal acetate we may conclude that the substance contains hydroxyl other than the hydroxyl of carboxyl.

EXPERIMENT. To 3 c.c. of absolute alcohol add 3 c.c. of acetyl chloride. HCl is evolved. Note the odour of ethyl acetate.

The above experiments, therefore, justify our writing the formula C_2H_3O-OH . Further corroboration of this is found in the fact that two molecules of acetic acid can be made to unite together with the loss of a molecule of water, thus:

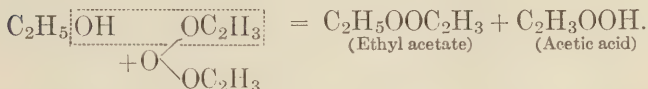


the resulting body being **acetic anhydride**. For practical purposes acetic anhydride may be prepared by acting on acetyl chloride with anhydrous sodium acetate, thus:



It is a fluid giving off a suffocating vapour. Added to water, it sinks to the bottom of the vessel, but gradually becomes reconverted into acetic acid. Its

readiness to re-form acetic acid causes it to attack the hydroxyl group of alcohols and other hydroxyl compounds, one of the acetyl groups becoming thereby attached in place of the OH group, thus:



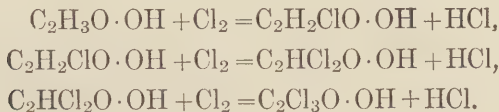
Like acetyl chloride, it may therefore be employed for ascertaining whether a substance contains hydroxyl not in carboxyl, and if so, how many such groups it contains (see p. 179).

(3) There remains for us to find out *how the acetyl radicle* $\text{C}_2\text{H}_3\text{O}$ *is composed*. A clue to this is furnished by the observation that methane, CH_4 , and a carbonate are obtained by heating anhydrous sodium acetate with soda-lime (see exp., p. 96):



This must mean that the two carbon atoms are of different value and that one of them exists in combination with hydrogen as methyl, CH_3 .

Further corroboration of this is furnished also by the fact that the three H atoms which belong to the methyl group can be separately replaced by chlorine atoms, thus forming the substitution products *mono-, di-, or tri-chloroacetic acid*:



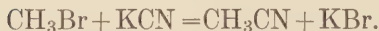
The resulting substitution products retain the acid properties of acetic acid, such as the power of forming ethereal salts, anhydrides, etc. The chlor-acetic acids are much stronger acids than acetic acid, and the acid power increases with increase in the number of chlorine atoms.

(4) If we represent acetic acid as containing a methyl group its formula must be written either CCH_3OOH , COCH_3OOH , or CH_3COOH : which of these is correct? The valence of carbon prevents C of CH_3 having more than one linking to the rest of the molecule, also for the other C to satisfy its valence it is necessary that it be linked to both oxygen atoms as well as to C of CH_3 , therefore, the structure must be CH_3COOH . *Further evidence that the group COOH does actually exist in acetic acid* is given by the following observations:

(a) The formation of sodium acetate by treating sodium methyl with CO_2 : $\text{CH}_3\text{Na} + \text{CO}_2 = \text{CH}_3\text{COONa}$.

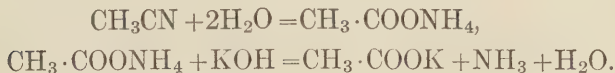
(b) The result of electrolysis of acetic acid. The cation H^+ is liberated at the cathode; the anion CH_3COO^- passes to the anode, where it is liberated as CO_2 and ethane (the two methyl (CH_3) groups from two molecules having united together).

(5) By synthesis, as shown by the equations:



EXPERIMENT. Take 2 gm. of acetonitrile (prepared as directed in the experiment under methyl cyanide, see p. 184) and mix with 10 c.c. of 60% KOH in a

small flask. Attach the flask to an upright (reflux) condenser. Heat for forty-five minutes. Note the ammonia escaping from the top of the condenser. Neutralize the resulting fluid with HCl and test for acetic acid (see previous experiments):



*THE CAUSE OF THE RELATIVE STRENGTHS OF ACIDS
(AND BASES).*

It is important to understand what it is that constitutes the strength of an acid or alkali. This obviously cannot be gauged by titration with indicators: a normal solution of *any* acid will be neutralized by an equal volume of a normal solution of any alkali, and yet such acids as HCl, H₂SO₄, etc., are far more *reactive*—are stronger, in other words—than such acids as acetic, lactic, etc. This difference in strength is explained by the fact that only a certain fraction of any acid or alkali is effective, the value of this fraction being proportional to the strength of the acid or alkali. The effective fraction of an acid is that portion of it which becomes ionized. In solution, acids ionize into a cation of hydrogen or hydrion (which being charged with + electricity is often called the positive ion) and an anion of the rest of the molecule (see p. 58). In the case of solutions of strong acids a much greater proportion of acid ionizes in this way than in the case of an equimolecular solution of weak acids. We may therefore state that the *active acidity of a solution of an acid depends on the concentration of the hydrogen ions.*

(See the table in the appendix, p. 409, for dissociation constants of a number of organic acids.)

In the case of bases, e.g., KOH, NH_4OH , dissociation in solution into cations of the metal or its equivalent (K , NH_4) and into anions of hydroxyl occurs. It is the concentration of the *hydroxyl ions* (hydroxions) which determines their strength (cf. amines, p. 189).

(See the table in the appendix, p. 409, for dissociation constants of certain bases.)

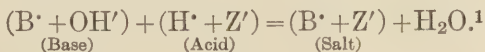
In a solution of HCl, for example, there exist: (a) undissociated HCl, (b) cations of H^+ , and (c) anions of Cl' ; in a solution of acetic acid: (a) undissociated $\text{CH}_3\cdot\text{COOH}$, (b) cations of H^+ , and (c) anions of $\text{CH}_3\text{COO}'$: but the amount of (a) in the two cases will be very different, there being much less dissociation (i.e., (a) is of greater value) in the case of acetic acid than in the case of hydrochloric acid. In every acid, therefore, there must exist a certain proportion between the undissociated and the dissociated portions. This will, of course, vary at different dilutions, for it will be remembered that dissociation increases with dilution (see p. 61). Since it is known that the electrical conductivity of a solution depends on the amount of dissociation of the electrolyte dissolved in it, we may obtain a value for this proportion by measurement of electrical conductivity.

ETHEREAL SALTS. ESTERS.

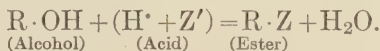
Corresponding to the salts of inorganic chemistry there are derivatives of organic acids in which the hydrogen of carboxyl is replaced by some hydrocarbon radicle. Thus ethyl acetate has the formula

$\text{CH}_3\text{COO} \cdot \text{C}_2\text{H}_5$, from which it is seen that the two constituent radicles are linked together through an oxygen atom as in the ethers (see p. 109). On this account such compounds are usually called *ethereal salts* or more briefly *esters*. In a looser sense, compounds of mineral acids with organic radicles, as ethyl nitrate, $\text{C}_2\text{H}_5\text{ONO}_2$, and ethyl sulphate, $(\text{C}_2\text{H}_5)_2\text{SO}_4$, are included in this group; but since such as these have been considered elsewhere we shall study at present only those salts in which both basic and acid portions are organic.

Inorganic salts are immediately formed when solutions of an acid and a base are mixed together, for, both of these being ionized, the hydrogen ion of the acid immediately unites with the hydroxyl ion of the base to form water:



Esters are, however, not thus readily formed, for the reacting hydroxide, being an alcohol, is not ionized, but remains as a molecule, and on this the acid only slowly acts:

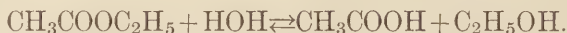


Not only are inorganic distinguished from ethereal salts in their ease of formation but also in their dissociability in solution, the former being usually entirely dissociated in solution, the latter not at all so. In

¹ This equation will serve as an example of how ions are represented in a reaction.

this connection it is of great importance to point out that salts of organic acids with metals do undergo dissociation in solution and to about the same extent as inorganic salts. Thus in a solution of ethyl acetate there are no free ions, whereas in one of sodium acetate dissociation into Na^+ and $\text{CH}_3\text{COO}'$ ions occurs.

Mass Action. One of the notable illustrations of mass action is ester formation. The formation of an ethereal salt when an alcohol and an acid are directly mixed, although slow, yet proceeds until a balance between the four constituents is established (i.e., between acid, alcohol, salt, and water). This is because the reaction is a reversible one; in other words, whenever a slight excess of water comes to exist in the mixture, it decomposes the ester into the acid and alcohol, thus:



Such *reversible reactions* are often represented in equations by two arrows in place of the sign of equality.

The mixture comes to a point of equilibrium when 0.669 part of a gram molecule of ester is present, provided we started with one gram-molecule of both acid and alcohol. At the beginning of the reaction the mass action of both alcohol and acid is most marked, forcing ester production, the reverse action being very slight. As ester and water accumulate, ester formation slows up and the reverse action begins to figure in the reaction, until finally the mass action of the water to cause hydrolysis is as pronounced as that of the alcohol and acid to cause esterification. The equilibrium is not really static, the action and the reverse action are going on constantly to an equal degree thus maintaining a balance.

The amount of ester thus formed depends on the relative amounts of acid and alcohol present and not on the temperature. With a given amount of alcohol an increase in the amount of acid increases the yield of ethereal salt, and, conversely, the same is true with a given amount of acid when more alcohol is used. Since the progress of the formation of the above ester can be followed by titrating the residual acid, the reaction has been extensively employed in studying the laws of mass action.

The fundamental law of mass action states that the product of the number of gram-molecules per litre of the substances on the one side of the equation divided by the product of these on the other side is equal to some constant. In the case of the above reaction we have therefore the equation

$$\frac{C \text{ acid} \times C \text{ alcohol}}{C \text{ ester} \times C \text{ water}} = \text{constant},$$

where C represents gram-molecules per litre of the reacting substances.

It will be evident that if we increase C acid while C alcohol remains constant, then C ester must increase, which leads us to the conclusion that if enough acid be added all the alcohol will become converted into ester, or, conversely, that if more alcohol be added, the acid remaining constant, the same will be true. For example if one gram-molecule of acetic acid and two gram-molecules of ethyl alcohol interact they come to equilibrium when 82.9% of a gram-molecule of ethyl acetate is formed.

Temperature does not effect the constant to any marked degree, i.e., does not influence the ultimate amount of ethereal salt produced. On the other hand, it greatly influences the rate of reaction, i.e., the time that it takes for the condition of chemical equilibrium to be reached. Thus a rise in temperature increases the velocity of the reaction (as a rule the rate doubles for each increase of ten degrees in temperature). At 55° cane sugar is hydrolyzed by acids about five times as fast as at 25°. By studying different alcohols and acids, it has been found that if equimolecular amounts of acid and alcohol be used the limit of esterification, i.e., the constant, varies only slightly,¹ but the rate is much greater for such acids as acetic than it is for such as benzoic, and for primary than for secondary alcohols.

The amount of ester produced can be greatly increased by removing the water formed during the reaction, and in some cases this can be accomplished. By removing the ethereal salt as it is formed (e.g., by distillation or crystallization) much higher yields can also be obtained (see exp., p. 156).

Preparation of Ethereal Salts. The more usual methods for preparing ethereal salts are the following:

1. By heating a mixture of the acid and alcohol with sulphuric acid: ethylsulphuric acid is first formed

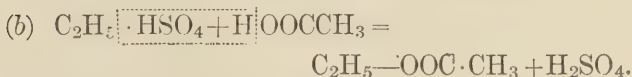
¹ For example the per cent of a gram-molecule of ester formed by some alcohols and acids is as follows:

Acetic acid+methyl alcohol 67.5, benzoic acid+methyl alcohol, 64.5.

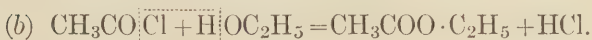
Acetic acid+ethyl alcohol 66.9, benzoic acid+ethyl alcohol 67.

Acetic acid+amyl alcohol 68.9, benzoic acid+amyl alcohol 70.

and then reacts with the acid, sulphuric acid being re-formed (*cf.* ether, p. 91), thus:

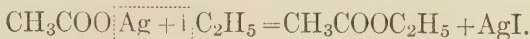


2. By heating a mixture of the acid and alcohol with hydrochloric acid gas: an acid chloride is probably first formed, which then reacts with the alcohol:



3. Or the second stage of this reaction (b) can be itself used for the production of ethereal salts by treating an alcohol with an acid chloride or an anhydride of an acid. In this latter manner the acetyl or benzoyl (see p. 144) derivatives of many substances can be produced, and these, being readily purified, are extensively prepared for purposes of identification. The addition of sodium hydroxide accelerates this reaction in the case of benzoyl compounds (see p. 321).

4. By treating a silver salt of an acid with an alkyl halide (as iodide):



Properties. Esters in a pure state are stable; in watery solution they slowly decompose into acid and alcohol, the decomposition being greatly accelerated by boiling with water and by the action of acids or

bases. Hydrolysis¹ most readily occurs with those esters which are easily formed; thus methyl acetate is more readily formed and is more easily hydrolyzed than ethyl acetate.

Many esters have pleasant odours, often simulating those of fruits, for instance isoamyl acetate has an odour resembling pears. On this account some of them are used as artificial fruit essences (see p. 161).

Ethereal salts include the *neutral fats* (see p. 176). The two most important ethereal salts of acetic acid are methyl and ethyl acetates. Prepared by the general methods described above, both these bodies are liquids with pleasant odours. Ethyl acetate is commonly called acetic ether.

From a bio-chemical standpoint the acceleration which acids induce in the hydrolysis of esters is of interest, partly because a method for the quantitative determination of the acid in gastric juice is based on it, and partly because it typifies *catalytic action*, which is the means possibly by which ferments produce their actions.

Catalysis is defined as consisting in acceleration or retardation of reactions which would take place without the catalyzer, but more slowly. Neither the acid molecule nor the ions enter into the chemical reaction. When a chemical agent enters into the reaction and is recovered, as sulphuric acid in ether production, it is a *pseudo-catalyst*.

If equimolecular quantities of different acids be added to similar quantities of methyl acetate, it will be found that the acceleration of hydrolysis produced

¹ Hydrolysis of esters is commonly called *saponification* (see p. 181).

varies greatly with the acid employed. HCl and HNO_3 produce about the greatest acceleration, whereas the commonest organic acids have only a feeble influence; thus the accelerating influence of oxalic acid is only 19% and of acetic only 0.4% of that of HCl (see table in appendix, p. 410). Now it has been found that the electrical conductivity of dilute solutions of the acids is directly proportional to their accelerating (catalytic) power, which leads us to the conclusion that the catalytic power depends on the amount of dissociation which the acids undergo; in other words, on the number of hydrogen ions existing in the solution (see p. 148).

By this means, therefore, we have a practical method for gauging the relative strengths of acids (see p. 158).

Further, if we add dilute solutions of varying concentrations of the same mineral acid to methyl acetate it will be found that the rate of saponification is proportional to the strength of acid added. It is important to note that this law holds only for dilute solutions (less than decinormal) of strong acids and not at all for weak acids. By comparing the amount of saponification of methyl acetate which occurs when a known quantity of acid is added, with the amount occurring in a similar solution of methyl acetate having an unknown quantity of the same acid, an estimate can be made of the amount of acid actually present in the latter. In this comparison the two solutions must of course be kept at the same temperature and the action allowed to proceed for the same length of time (see exp. below).

EXPERIMENTS. (1) Put into a medium-sized flask 10 c.c. of alcohol and 10 c.c. of C.P. H_2SO_4 . Use a three-hole cork; by one hole suspend a dropping funnel, by

another connect with a condenser, also insert a thermometer so that its bulb is in the liquid. Heat until the liquid is at 135° , then begin running in slowly by the dropping funnel a mixture of 80 c.c. of alcohol and 80 c.c. of glacial acetic acid, keeping the temperature of the mixture constant at about 135° . Regulate the inflow of acid alcohol to about correspond to the rate of distillation. Wash the distillate in the receiving flask with small portions of saturated sodium carbonate solution until the top layer is no longer acid to litmus. Separate with a separating funnel. Add to the acetic ether a cold solution of 20 gm. of calcium chloride in 20 c.c. of water and shake. (The ester is soluble in 17 parts of water). Separate with the funnel. Put the ethyl acetate into a dry flask, add solid calcium chloride, cork, and let it stand a day or so. Redistil on a water bath, noting the boiling-point (77°). Determine the specific gravity (0.905 at 17°).

(2) Determine the rate of saponification of methyl acetate as influenced by different strengths of acid (HCl). Into each of two small flasks put 1 c.c. of methyl acetate measured accurately with a pipette; to one add with a pipette 20 c.c. of HCl solution of known strength (say 0.4%); to the other add 20 c.c. of HCl more dilute but of unknown concentration; cork each flask and shake. As quickly as possible titrate 5 c.c. of each mixture successively with decinormal NaOH, using phenolphthalein as an indicator. This gives the acidity of each at the beginning of the experiment. Cork the flasks tightly with rubber stoppers and keep them in an incubator at about 40° for three or four hours, then, after shaking and cooling, take 5 c.c. from each and titrate

again. The increase in acid (due to acetic acid liberated by saponification) is found by deducting the initial titration from this second titration. The stronger solution causes the greater amount of saponification. To calculate the exact strength of the unknown acid solution by comparison with the known we must find out the limit of saponification for the known strength; to do this leave the flask containing this acid in the incubator for forty-eight hours, then titrate again. The titration at the end of this period, less the initial titration, gives an acid value called A ; this is the number of cubic centimetres of decinormal acetic acid that can be liberated by saponification of the methyl acetate by 0.4% HCl. Now we can reckon the per cent of HCl in the other solution in the following manner: Find the value of the constant in the formula $C = \log \left(\frac{A}{A-X} \right)$ for each solution, but call the constant of the known solution C' . The observed increase in acid content during the three or four hours' incubation is X .

Take a particular experiment. A known solution (0.43435% HCl) gave $A = 24.9$ (c.c.). The increase (after four hours) in the known solution was 12.1 (c.c.), therefore $A - X = 24.9 - 12.1 = 12.8$:

$$C' = \log \left(\frac{24.9}{12.8} \right) = .2878.$$

With the unknown solution $X = 7$ (c.c.), $A - X = 17.9$:

$$C = \log \left(\frac{24.9}{17.9} \right) = .1430.$$

Now the per cent of HCl in the unknown

$$= \left(\frac{C \text{ of unknown}}{C' \text{ of known}} \right) (\text{per cent HCl in known}).$$

$$\text{Therefore per cent} = \left(\frac{.1430}{.2878} \right) (0.43435) = 0.21544.$$

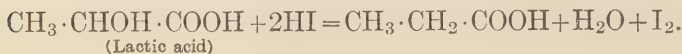
In this particular case the unknown was of exactly half the strength of the known solution.

The rate of saponification bears a definite relation to the number of hydrogen ions present in the solution. Therefore with dilute solutions of easily ionizable acids (which are completely dissociated), as most mineral acids, an accurate estimation of the quantity of acid present can be made by this method. Most organic acids furnish so few hydrogen ions (see p. 133) that their presence has practically no effect. In consequence, the method is available for determining the per cent of HCl present in gastric juice or stomach contents.

It must not be forgotten, however, that the presence of salts (as in stomach contents) can change the rate of saponification from what it would be if only pure acid were present.

OTHER FATTY ACIDS.

Propionic acid (propanoic acid), $\text{CH}_3 \cdot \text{CH}_2 \cdot \text{COOH}$, resembles acetic acid. It can be prepared in similar ways as the latter, namely, by oxidation of propyl alcohol, by hydrolysis of ethyl cyanide, and by the action of CO_2 on sodiummethyl. In addition it can be made by reduction of lactic acid, thus:



The hydriodic acid furnishes nascent hydrogen, and this brings about reduction.

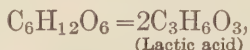
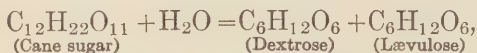
Corresponding to chloracetic acids there are chlorpropionic acids. But the halogen may take the place of hydrogen either in the CH_3 group or in the CH_2 group of propionic acid. It becomes necessary, therefore, to distinguish between these two positions in the molecule. This is done by using Greek letters, α and β . In order to have a rule which will apply to all acids, no matter how many carbon atoms the acid may contain, it is necessary to count backwards from the carboxyl group: thus, the group next to the COOH is in the α position, the second group is in the β position, and so on; for example, $\text{CH}_3 \cdot \text{CHCl} \cdot \text{COOH}$ is α -chlorpropionic acid, $\text{CH}_2\text{Cl} \cdot \text{CH}_2 \cdot \text{COOH}$ is β -chlorpropionic acid.

Butyric acid (butanoic acid), $\text{CH}_3 \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{COOH}$, is normal butyric acid.

Isobutyric acid or methylpropanoic acid has the formula $\begin{matrix} \text{CH}_3 \\ \text{CH}_3 \end{matrix} \rangle \text{CH} - \text{COOH}$. Normal butyric acid is fermentation butyric acid, and occurs in Limburger cheese, rancid butter, and sweat. It may be prepared by oxidation of butyl alcohol and by hydrolysis of propyl cyanide. Butter contains about six per cent of butyrin, which is the glycerol ester of butyric acid (see p. 174); the acid can therefore be obtained by hydrolysis or saponification of butter (see exp., p. 180). Microorganisms can cause fermentation of butter, with resulting hydrolysis of the ester (butyrin) and setting free of butyric acid. Butyric acid is soluble in water and volatile. Oleomargarine contains very little butyric or other soluble volatile fatty acids. On this account it

can readily be identified by making an estimation of the volatile acids in the manner to be described later in an experiment (see p. 180).

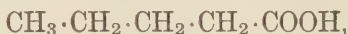
Butyric acid can also be made from cane sugar as follows: The sugar solution, acidified with tartaric acid, is inoculated with sour milk: one variety of micro-organisms in the latter "inverts" the sugar into dextrose and lævulose; another variety ferments these monosaccharides, producing lactic acid; while a third variety converts the lactic acid into butyric acid.



Similar fermentation, with production of lactic and butyric acids, may occur in the stomach when the hydrochloric acid of the gastric juice is deficient in amount or absent altogether. The gases formed (CO_2 and H_2) cause the flatulence present in such cases. Butyric acid has the peculiar disagreeable odour characteristic of rancid butter.

The ethereal salt $\text{C}_3\text{H}_7 \cdot \text{COOC}_2\text{H}_5$, **ethyl butyrate**, resembles pineapple in odour. It is used as a flavouring material in place of pineapple juice.

Valeric acid (valerianic acid),



is the normal acid. Ordinary valeric acid, however, is isovaleric acid, $\begin{matrix} \text{CH}_3 \\ \text{CH}_3 \end{matrix} \rangle \text{CH} \cdot \text{CH}_2 \cdot \text{COOH}$. It occurs in valerian root.

Amyl valerate, $C_4H_9 \cdot COOC_5H_{11}$, smells like apple, and is therefore used as an apple essence. This is the ester of isoamyl alcohol with isovaleric acid. It has been used as a medicine.

Of the other acids of the formic acid series, only those containing an even number of CH_2 groups are of importance.

Caproic acid is $CH_3(CH_2)_4COOH$.

Caprylic acid is $CH_3(CH_2)_6COOH$.

Capric acid is $CH_3(CH_2)_8COOH$.

Lauric acid is $CH_3(CH_2)_{10}COOH$.

Myristic acid is $CH_3(CH_2)_{12}COOH$.

Palmitic acid is $CH_3(CH_2)_{14}COOH$.

Stearic acid is $CH_3(CH_2)_{16}COOH$.

Arachidic acid is $CH_3(CH_2)_{18}COOH$.

Behenic acid is $CH_3(CH_2)_{20}COOH$.

Most of these occur in fats. The lowest acids are volatile with steam and soluble. The higher acids are non-volatile and insoluble. The melting-point of palmitic acid is 62.6° , and of stearic acid is 69.2° .

The calcium salt of moniodo behenic acid is a remedy called *sajodin*; it is used for administration of iodine.

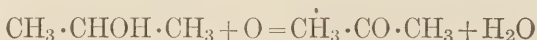
CHAPTER XIII.

SECONDARY AND CERTAIN OTHER MONACID ALCOHOLS. KETONES

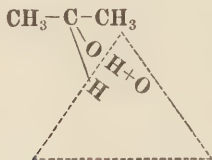
SECONDARY ALCOHOLS AND THEIR OXIDATION PRODUCTS.

SECONDARY alcohols contain the group CHOH , as in $\text{CH}_3 \cdot \text{CHOH} \cdot \text{CH}_3$, *secondary propyl alcohol*. None of the secondary alcohols is of any importance.

When a secondary alcohol is oxidized an aldehyde is not formed, but a *ketone*:



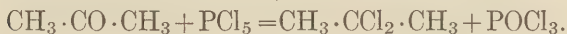
or



A **ketone** is in all essential points identical with an aldehyde, the only difference being that in the case of an aldehyde the oxygen atom is attached to a carbon atom at one end of the chain, while in a ketone it is attached to an inner carbon atom. Furthermore many ketones act as reducing agents toward alkaline silver and copper solutions. Some ketones give the fuchsin

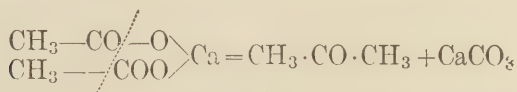
test (see p. 130), particularly those that have $\text{CH}_3 \cdot \text{CO}$ — in the molecule. Many ketones form addition compounds with acid sulphites and with hydrocyanic acid (*cf.* aldehydes). Ketones do not polymerize, but they form condensation products.

The reaction of phosphorus pentachloride with ketones is similar to that with aldehydes:



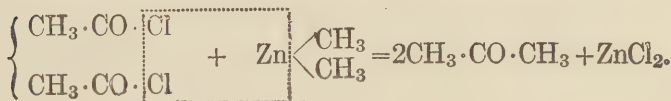
No hydrochloric acid is produced and a dichlor derivative is formed, therefore *a ketone does not contain hydroxyl*. The most important ketone is acetone.

Acetone (dimethylketone or propanone), $\text{CH}_3\text{CO} \cdot \text{CH}_3$, is the simplest ketone. It is produced by the dry distillation of calcium acetate.



Commercially, it is prepared from crude wood alcohol (see p. 139).

It can also be obtained by oxidation of secondary propyl alcohol. Its synthesis from zinc methyl and acetyl chloride proves the structural formula for acetone.



It is present in the urine under certain conditions, especially in severe cases of diabetes. It is a useful

solvent. Acetone is a liquid, boiling at 56.3° (corrected). Its specific gravity is 0.812 at 0° . Nascent hydrogen converts it into secondary propyl alcohol. It does not oxidize to an acid containing the same number of carbon atoms, but to acetic and formic or carbonic acids. Acetone gives the iodoform test.

EXPERIMENTS. (1) Make iodoform, using acetone instead of alcohol (see p. 107).

The reactions involved are of the same nature as in the preparation of iodoform from alcohol, in this case the intermediate compound is triiodoacetone, $\text{CI}_3 \cdot \text{CO} \cdot \text{CH}_3$.

(2) Dissolve 2 c.c. of acetone in dilute H_2SO_4 ; add KMnO_4 solution until a pink colour remains on warming. Filter, make the filtrate strongly acid with 20% H_2SO_4 , and distil. Test the distillate for acetic acid (see p. 140).

(3) Shake 5 c.c. of acetone with 8 c.c. of a saturated solution of sodium bisulphite; cool; crystals of the addition compound of acetone appear. Filter and wash. Save samples.

Chloretone (chloroform acetone, trichlor-tertiary-butyl-alcohol), $\text{CH}_3-\text{C} \begin{array}{l} \nearrow \text{O}-\text{H} \\ \longrightarrow \text{CCl}_3 \\ \searrow \text{CH}_3 \end{array}$, is an addition prod-

uct of acetone. It is formed by the interaction of acetone and chloroform in the presence of an excess of KOH . It is a useful hypnotic.

Brometone, the corresponding bromine preparation, produced from acetone and bromoform, is analogous

to chloretone. As a remedy it is used instead of bromides.

Sulphonal, another hypnotic, is produced from acetone (see p. 194).

Some acids are ketone acids containing both the carbonyl and carboxyl groups. **Aceto-acetic acid**, $\text{CH}_3 \cdot \text{CO} \cdot \text{CH}_2 \cdot \text{COOH}$, typifies these and is of importance, since it may occur in the urine (see p. 202).

Tertiary alcohols, when oxidized, decompose into compounds containing fewer carbon atoms than the alcohol. The tertiary alcohols are of no importance.

Little need be said of other monacid alcohols, except that most **waxes** contain esters of monacid alcohols having a large number of carbon atoms—for example, ceryl alcohol, $\text{C}_{26}\text{H}_{53}\text{OH}$, cetyl alcohol, $\text{CH}_3(\text{CH}_2)_{14}\text{CH}_2\text{OH}$, and melissic alcohol, $\text{C}_{30}\text{H}_{61}\text{OH}$.

In waxes some of the alcohol is not in ester combination, but free.

Cetyl palmitate has been found in the fat of an ovarian cyst. Lanolin contains some wax esters (see p. 183).

CHAPTER XIV.

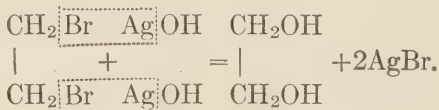
DIACID ALCOHOLS AND DIBASIC ACIDS.

DIACID ALCOHOLS.

DIACID alcohols contain two hydroxyl groups. They are comparable to $\text{Ca}(\text{OH})_2$. The simplest diacid alcohol and the only one of importance is **glycol** (ethandiol), CH_2OH

$\begin{array}{c} | \\ \text{CH}_2\text{OH} \end{array}$. The method of preparation shows that both

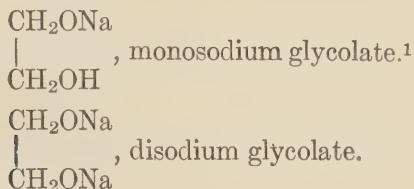
hydroxyl groups are not attached to the same carbon atom. Ethylene is produced from ethyl alcohol by heating the latter with an excess of sulphuric acid. The ethylene is saturated with bromine, forming ethylene bromide, in the manner described in the experiment (see p. 269). From ethylene bromide glycol can be obtained by the action of silver hydroxide:



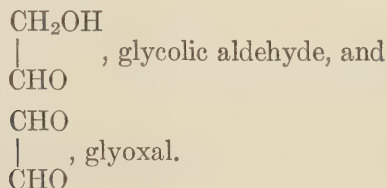
Glycol is a colourless glycerol-like liquid, of sweetish taste. It boils at 195° and has a specific gravity of 1.128 at 0° .

It forms two classes of ethereal salts, according to

whether one or both hydroxyls are replaced. Similarly there are two sodium alcoholates of glycol:

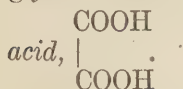


The oxidation products of glycol are numerous because of the presence of two primary alcohol groups. There are two aldehydes:



Oxidation of the first gives rise to *glycollic acid*, $\begin{array}{c} \text{CH}_2\text{OH} \\ | \\ \text{COOH} \end{array}$; this will be considered under hydroxy-acids (see p. 196).

Oxidation of glyoxal gives $\begin{array}{c} \text{CHO} \\ | \\ \text{COOH} \end{array}$, *glyoxylic acid*; this is really a dihydroxy-acid, as will be seen later (see p. 203). These two acids are monobasic. Complete oxidation of glycol results in the formation of a dibasic acid, *oxalic*



¹ Distinguish from the *glycollates* derived from glycollic acid (p. 197).

DIBASIC ACIDS.

The simplest is *oxalic acid*. The next members of the series are *malonic acid*, $\text{CH}_2 \begin{smallmatrix} \diagup \text{COOH} \\ \diagdown \text{COOH} \end{smallmatrix}$, *succinic acid*,

$\begin{smallmatrix} \text{CH}_2\text{—COOH} \\ | \\ \text{CH}_2\text{—COOH} \end{smallmatrix}$, and *glutaric acid*, $\text{CH}_2 \begin{smallmatrix} \diagup \text{CH}_2\text{—COOH} \\ \diagdown \text{CH}_2\text{—COOH} \end{smallmatrix}$.

General methods for the production of dibasic acids are (1) by hydrolysis of cyan-acids, (2) by oxidation of diacid alcohols, and (3) by oxidation of an hydroxy-acid.

The acids of the oxalic acid series show the same behaviour as regards melting-points as do the acids of the formic acid series (see p. 134).

Oxalic acid, $\begin{smallmatrix} \text{COOH} \\ | \\ \text{COOH} \end{smallmatrix}$, forms crystals containing two

molecules of water for each molecule of oxalic acid. The crystals readily effloresce. It may be prepared by oxidation of cane sugar with nitric acid. It is made commercially by heating sawdust with caustic potash and soda. After cooling the oxalate is dissolved out of the mass, precipitated by slaked lime as calcium oxalate, and the separated oxalate is treated with sulphuric acid, setting oxalic acid free. Oxalic acid is one of the strongest of all organic acids, because its solution contains more hydrogen ions than the corresponding solutions of most other organic acids (see p. 148).

As the number of C atoms interposed between the carboxyls of acids of this series is increased, acid power is decreased.

When oxalic acid is heated, it first loses its water of

crystallization, then decomposes into carbon dioxide, carbon monoxide, water, and some formic acid. If heated in the presence of glycerol, formic acid and carbon dioxide are formed (see p 136). Sulphuric acid decomposes it to carbon monoxide, carbon dioxide, and water. Potassium permanganate in warm acid solution oxidizes it to carbon dioxide and water:



Oxalic acid forms two classes of salts, acid and neutral. *Acid potassium oxalate*, $\begin{array}{c} \text{COOH} \\ | \\ \text{COOK} \end{array}$, occurs in plants,

particularly sorrel. *Ammonium*, *potassium*, and *sodium oxalates* are soluble; all other oxalates of metals are practically insoluble. *Calcium oxalate* frequently occurs in the urine as a crystalline sediment.

Oxalic acid is poisonous and has been used for suicidal purposes.

EXPERIMENTS. (1) *Preparation of oxalic acid*. Heat 200 c.c. of HNO_3 in a large flask to 100° . Set in a fumecloset and add 50 gm. of cane sugar. When the evolution of fumes has ceased, evaporate the acid mixture in an evaporating dish to about one fifth its original volume. Cool and collect the crystals. Recrystallize, using as little hot water as possible.

(2) Heat some dry crystals of oxalic acid in a test-tube—loss of water of crystallization occurs, as shown by drops collecting on the cool part of the tube.

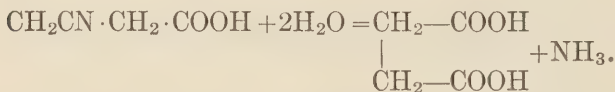
(3) Decompose some oxalic acid with H_2SO_4 ; test the

evolved gases for CO_2 (baryta water, as on p. 3) and CO (hæmoglobin solution, as on p. 137).

(4) To 5 c.c. of oxalic acid solution add a few drops of H_2SO_4 , warm, then add potassium permanganate solution—it is decolorized.

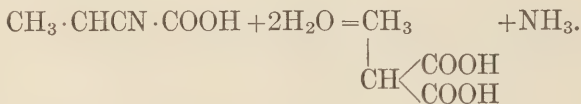
Malonic acid, $\text{CH}_2\begin{smallmatrix} \text{COOH} \\ \text{COOH} \end{smallmatrix}$, is of importance mainly in bringing about certain organic syntheses.

Succinic acid, $\begin{smallmatrix} \text{CH}_2\text{—COOH} \\ | \\ \text{CH}_2\text{—COOH} \end{smallmatrix}$, is *normal* succinic acid and may be produced by hydrolysis of β -cyanpropionic acid:



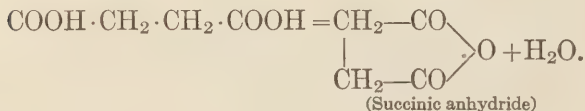
If caustic potash is used to effect hydrolysis, potassium succinate would be formed.

If α -cyanpropionic acid be hydrolyzed *isosuccinic* acid is formed:



These two acids give different reactions.

Normal succinic acid when heated to 235° yields *succinic anhydride* and water:

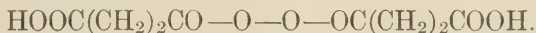


Isosuccinic acid, however, when heated above 130°, breaks up into propionic acid and carbon dioxide:



It is, indeed, a general rule in organic chemistry that two carboxyl groups cannot remain attached to the same carbon atom at high temperatures, carbon dioxide being split off from one of the carboxyls.

Alphozone (disuccinyl peroxide) is an organic peroxide) (cf. acetozone p. 316).



It is an oxidizing agent, and is said to be antiseptic.

CHAPTER XV.

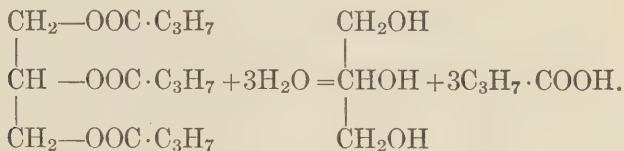
TRIACID ALCOHOLS, FATS, AND SOAPS.

TRIACID ALCOHOLS.

Glycerol (glycerine or propanetriol), $\begin{array}{c} \text{CH}_2\text{OH} \\ | \\ \text{CHOH} \\ | \\ \text{CH}_2\text{OH} \end{array}$, is the

only triacid alcohol of importance. Glycerol occurs in fats in combination with fatty acids and oleic acid, as glycerol esters of these acids. By hydrolyzing (i.e., saponifying) fats, glycerol is set free. This is accomplished commercially by heating fats (at 170–180°) in a closed boiler or autoclave with water and lime. The lime combines with fatty acids, forming insoluble calcium salts, while the glycerol goes into solution. The calcium remaining in solution is precipitated with sulphuric acid. The dilute glycerol solution is then evaporated under diminished pressure at as low a temperature as possible until its specific gravity becomes 1.24. The crude glycerol is purified by distillation with superheated steam. C.P. glycerol is prepared by treatment of distilled glycerol with animal charcoal and concentration by vacuum distillation.

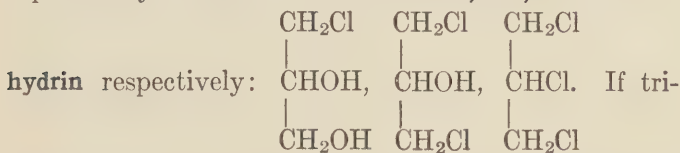
Glyceryl butyrate or butyirin yields on saponification glycerol and butyric acid, thus:



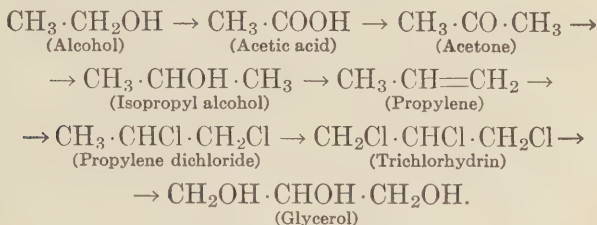
The other fats will be considered more fully presently.

Pure glycerol is a colourless, syrupy liquid, having a sweet taste. It boils at 290° and has a specific gravity of 1.265 at 15° . It is hygroscopic. Crystals of glycerol can be obtained by cooling to a low temperature (0°); these melt at 17° . It is volatile with water-vapour. It is useful as a solvent and as a preservative agent.

One, two, or three of the hydroxyl groups can be replaced by chlorine to form **mono-, di-, or trichlor-**



chlorhydrin be heated with water to 170° , it is hydrolyzed to glycerol. Glycerol can be obtained from ethyl alcohol by producing successively acetic acid, acetone, isopropyl alcohol, propylene, propylene dichloride, trichlorhydrin, and finally glycerol:



Glycerol forms salts with nitric acid. The trinitrate is **nitroglycerine** or nitroglycerol. It is made by mixing glycerol with sulphuric and nitric acids, keeping the

mixture cold. Its formula is
$$\begin{array}{c} \text{CH}_2\text{—O—NO}_2 \\ | \\ \text{CH—O—NO}_2 \\ | \\ \text{CH}_2\text{—O—NO}_2 \end{array}$$
 It ex-

plodes when suddenly heated or percussed, with the formation of nitrogen, nitric oxide, carbon dioxide, and water. It is a yellow, oily liquid. **Dynamite** consists of infusorial earth or other material impregnated with nitroglycerol, and may contain as much as 75% of the latter.

Nobel discovered that nitrocellulose (p. 262) will absorb nitroglycerin, forming a gelatinous mass. Such explosives as cordite and ballistite are prepared in this way.

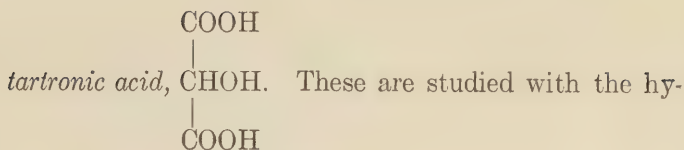
Gelatin dynamite is prepared from resin, collodion gun-cotton, a little wood pulp and nitroglycerol.

Nitroglycerol is a strong poison, causing violent headache and lowering of blood-pressure. In appropriate dosage it is extremely useful as a medicine.

Tetranitrol is similar to nitroglycerol, chemically and pharmacologically. It is the tetranitrate of the tetracid alcohol, erythrol.

Glycerol forms glyceryl acetates when treated with acetic anhydride. This will be considered more fully under fats.

On oxidation glycerol yields *glyceric acid*,
$$\begin{array}{c} \text{COOH} \\ | \\ \text{CHOH} \\ | \\ \text{CH}_2\text{OH} \end{array}$$
 and



droxy-acids (see pp. 203 and 205).

Glycerophosphoric acid consists of one molecule of orthophosphoric acid combined with glycerol, $\text{CH}_2\text{OH} \cdot \text{CHOH} \cdot \text{CH}_2(\text{H}_2\text{PO}_4)$.

EXPERIMENTS. (1) Heat 1 c.c. of glycerol with 5 gm. of KHSO_4 in an evaporating dish until it turns brown. Note the odour (acrolein) (see p. 271). The fumes will blacken a strip of paper that has been moistened with ammoniacal silver nitrate solution.

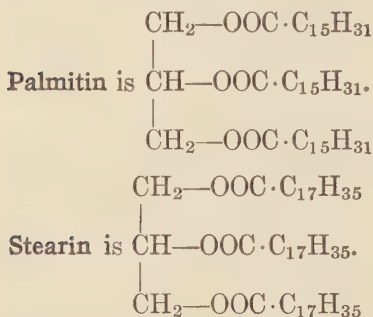
(2) Repeat the same experiment, using lard or some other fat. Glycerol in combination also gives the acrolein test.

(3) To a few cubic centimeters of NaOH solution add CuSO_4 until a copious precipitate of $\text{Cu}(\text{OH})_2$ is obtained; now add some glycerol and shake—a deep-blue solution results.

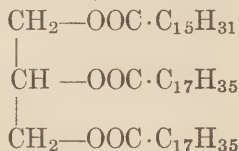
FATS AND SOAPS.

Fats contain esters of glycerol with fatty acids and with the unsaturated acid, oleic acid. Most fats are mixtures of *palmitin* (glyceryl tripalmitate), *stearin* (glyceryl tristearate), and *olein* (glyceryl trioleate). Olein is a liquid. Butyrin, caproin and caprylin are fluid at ordinary temperature, caprin melts at 31° ; these are all present in butter. Palmitin melts at 65° . Stearin has the highest melting-point (about 72°). Mutton-fat contains a large percentage of stearin.

Lard contains esters of lauric, myristic and linoleic acids, as well as the commoner esters. The softer fats contain less stearin and palmitin and relatively more olein. Physiologically, the fats of lower melting-point are more easily digested.



Mixed esters of glycerol can be obtained; some have been proven to occur naturally.



is a mixed ester.

The following esters have been detected in beef and mutton fat: dipalmito-stearin, dipalmito-olein, palmito-distearin and oleo-palmito-stearin.

Butter contains glycerol esters of fatty acids which are *volatile* and *soluble*, namely, butyric, capric, caprylic, and caproic acids. Artificial butters (as oleomargarine) contain only very small amounts of these acids.

Butter also contains esters of myristic, lauric and dihydroxystearic acids.

It will be of interest to give the composition of the oils that are used most commonly in medicine.

Cod-liver oil contains glycerides of palmitic, stearic, oleic, myristic, erucic and two other unsaturated acids, also cholesterol.

Croton oil contains tiglic, crotonic, formic, acetic, butyric, valeric, myristic and lauric acids, besides palmitic, stearic and oleic acids.

Castor oil is composed chiefly of esters of ricinoleic and isoricinoleic acids, and contains also sebacic, stearic and dihydroxystearic acids.

Olive oil has olein to the extent of seventy per cent, and contains also esters of palmitic and arachidic acids, and some phytosterol.

Fat Values. By determining certain analytical values¹ and by finding the melting-point and specific gravity, a fat can generally be identified with the aid of the tables compiled for the purpose. The values referred to will now be briefly explained in order.

(1) The *Reichert-Meissl value* indicates the amount of volatile soluble acid present in the fat. When butter or any other fatty substance is saponified so as to free the fat acid and then distilled as described in the experiment below, the volatile acid in the distillate can be readily estimated by titration. The Reichert-Meissl value is the number of cubic centimetres of decinormal acid contained in the distillate from five grams of fatty substance.

(2) The *acid value* of a fat is found by titration of a solution of the fat in alcohol ether mixture with decinormal KOH, using phenolphthalein as an indicator.

¹A very satisfactory book on this subject is *Chemical Analysis of Oils, Fats, and Waxes*, by J. Lewkowitsch.

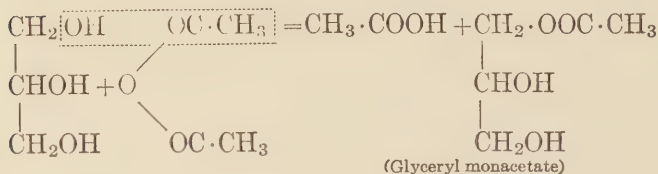
This determines the amount of free acid present. The acid value is expressed as milligrams of KOH required to neutralize the free acids in one gram of fat.

(3) The total amount of acid present, free and combined, is indicated by the *saponification value*. A weighed quantity of fat (2-4 gm.) is saponified by heating it with an accurately measured quantity of alcoholic KOH solution of known strength (half normal); the resulting soap is diluted and titrated with half normal HCl to find how much KOH remains unneutralized. Then the amount in milligrams of KOH combined with fatty acid as soap for each gram of fat taken is readily calculated; this is the saponification value.

(4) The *ester or ether value* of a fat represents the combined acid, being the saponification value less the acid value.

(5) The *iodine value* estimates the amount of unsaturated acid (e.g., oleic) present. The iodine forms an addition compound with the acid (see p. 268). This value is expressed as the grams of iodine taken up by 100 grams of fat.

(6) The *acetyl value* estimates the hydroxyl content. If glycerol be treated with acetic anhydride, one molecule of acetic acid is produced for each hydroxyl group attached (see p. 146):



The reaction can be pushed until all of the hydroxyl groups are displaced, giving, as the products, glyceryl triacetate and acetic acid (three molecules of the latter for each molecule of glycerol). In a similar manner a fat which contains some hydroxyl groups can be "acetylated," and by estimating the acetic acid in combination with the alcohol, or acids of the fat, the hydroxyl content can be calculated. Partially hydrolyzed fat esters (e.g., a diglyceride) and hydroxy acids are mainly responsible for this value. Such an acid is ricinoleic acid (p. 272) contained in castor oil, also dihydroxystearic acid, $\text{CH}_3(\text{CH}_2)_7(\text{CHOH})_2(\text{CH}_2)_7\text{COOH}$, which is present in butter and in castor oil.

EXPERIMENTS. (1) Compare the specific gravity of filtered butter and oleomargarine by successively putting a little of each in alcohol of specific gravity 0.926 at 15°. There must be no air bubbles adhering to the fat. The oleomargarine will float (it having a specific gravity of about 0.918 at 15°); the butter will either sink or remain suspended.

(2) *Reichert-Meissl value*. Into a 300 c.c. flask put 5 gm. of filtered butter, 2 c.c. of 60% KOH solution, and 20 c.c. of glycerol. Heat with a small flame, shaking to prevent excessive foaming. In about 5 minutes the water is boiled off and saponification is almost complete. Tip the flask and rotate to bring down any fat adhering to the walls. Heat again for a few minutes, then partly cool. The soap solution should be clear. Add 90 c.c. of hot distilled water and shake until the soap is dissolved. Add 50 c.c. of 5% H_2SO_4 and some small pieces of pumice.¹ Distil on a sand

¹ To prevent bumping.

bath. Collect 110 c.c. of distillate in a graduated flask. The distilling should be accomplished in 30 minutes. Filter the distillate; take 100 c.c. of the filtrate with a pipette and transfer it to a beaker. Add a little phenolphthalein solution and titrate with decinormal KOH until slightly pink. Multiply the number of cubic centimeters of alkali by 1.1; this gives the Reichert-Meissl value. For butter this value should not be less than 24. The experiment may be repeated with oleomargarine.

(3) *Acid value.* Mix equal volumes of alcohol and ether, add phenolphthalein solution, then a drop or more of decinormal KOH until slightly pink. Now dissolve a weighed quantity of butter (5–10 gm.) in some of the ether-alcohol, and titrate with decinormal KOH to a faint pink which remains after mixing. If the mixture becomes turbid during titration warm it in a water bath.

When fats are hydrolyzed with the aid of alkali, **soap** is formed. Hence the origin of the term *saponification*. In the strict sense, saponification means hydrolysis of an ester, the resulting products being an alcohol and an acid. Many use the word loosely as synonymous with hydrolysis.

Soaps are metallic salts of the acids which occur in fats. Ordinary soaps are mixtures of potassium or sodium palmitate, stearate, and oleate. Potassium soap is soft soap, commonly dispensed as green soap. It is of a yellow colour, but in many countries this colour is changed to green by the addition of indigo. It contains the glycerol that is freed by saponification. Sodium soap is hard soap. It is freed of glycerol by "salt-

ing out" in the manner described in the experiment. Castile or Venetian soap, if genuine, is made from olive oil. It contains no free alkali. It is slightly yellow in colour. Calcium, mercury, lead, copper, and many other metals form insoluble soaps.

Cheap soaps are made with resin, sodium resinate acting similarly to true soap.

The *cleansing action* of soap is due to the presence of free alkali in dilute soap solution. Hydrolytic dissociation of soap can be demonstrated as follows: Add phenolphthalein to a concentrated soap solution, and only a slight red colour appears; now dilute with a large quantity of water, when a decided red colour develops (for effect of dilution on dissociation, see p. 60). Thus the dilute soap solution used for washing contains just the right concentration of alkali to do the work and not enough alkali to be injurious. Dirt is held on the skin or clothing by the aid of fatty material; the alkali partly saponifies and partly emulsifies this, with the result that the "grease" can now be rinsed off. The lather also aids mechanically in removing dirt.

EXPERIMENTS. (1) Melt in an evaporating dish about 10 gm. of lard or tallow, add 100 c.c. of 20% KOH and 50 c.c. of alcohol, and boil moderately. After boiling half an hour test by shaking a drop of the fluid with half a test-tube of water; if no oily drops separate out, saponification is complete. Boil until completely saponified, adding water as necessary to maintain constant volume. While hot add an equal volume of saturated solution of NaCl. Sodium soap will separate as a top layer and finally solidify.

(2) To same soap solution add hydrochloric acid. Free fatty acids separate and rise to the top. Collect the fatty acids on a filter, wash thoroughly with water, press between filter paper, and crystallize from hot alcohol.

(3) Make insoluble soap by treating same soap solution with calcium chloride solution (calcium soap), with lead acetate (lead soap), copper sulphate, and solutions of other metallic salts.

Lanolin is a fat-like substance prepared by purifying wool grease. It contains about 25 per cent of water and will take up more water until it holds 80 per cent. It is more closely related to waxes than to fats, since its esters yield monacid alcohols, such as ceryl alcohol, by saponification. In addition to esters it contains free acids, free alcohols, cholesterol and ischolesterol.

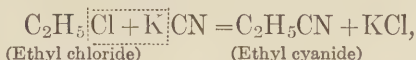
CHAPTER XVI.

NITROGEN DERIVATIVES. (ALSO PHOSPHORUS AND SULPHUR COMPOUNDS.)

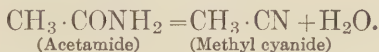
NITROGEN DERIVATIVES.

THESE fall into three classes: (1) cyanogen derivatives, (2) substituted ammonias, and (3) nitro compounds.

Cyanogen Derivatives. Organic cyanides can be prepared by treatment of alkyl halides with potassium cyanide, as



also by anhydrolysis (removal of water) of an acid amide (see p. 218), thus (see exp.):



EXPERIMENT. Into a dry 250 c.c. wide-mouth Jena flask (extraction flask) put 10 gm. of dry acetamide and add quickly about 15 gm. of phosphorus pentoxide. Mix quickly with a dry rod. As soon as possible add 10 gm. more of the oxide as a top layer. Cork and connect with a condenser immediately. Heat with a small smoky flame. Collect the distillate in a large clean test-tube. Shake the distillate with half its

volume of water, then add small pieces of solid KOH until no more dissolves, keeping the solution cool with running water; the cyanide now separates as a top layer. Remove the cyanide carefully with a clean dry pipette. Use the product for synthesis of acetic acid (p. 147).

The CN group of organic cyanides can be hydrolyzed to COOH; in consequence the alkyl cyanides are called acid *nitriles*; for example, $\text{CH}_3\cdot\text{CN}$ is acetonitrile because acetic acid can be obtained from it (see exp., p. 148):

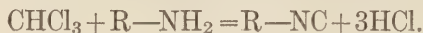


HCN , *hydrocyanic acid*, may be called formonitrile because it can be hydrolyzed to formic acid. As regards acid power it is extremely weak; its dissociation constant is less than one ten-thousandth of that of acetic acid. It is very poisonous, but is used in dilute solution as a remedy.

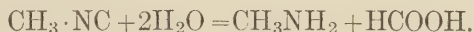
This reaction also shows that the carbon atom of CN is linked directly to the carbon chain. There are cyanides, however, in which it is the nitrogen atom of the CN group that is linked to the carbon chain. These are **isocyanides** or **isonitriles**. $\text{CH}_3-\text{N}\equiv\text{C}$ is *methyl isocyanide*.

Some chemists think that hydrocyanic acid may be a mixture of HCN and HNC , and that the metallic cyanides are mainly isocyanides.

Chloroform when heated with alkali and a primary amine gives rise to the disagreeable vapour of isocyanide:



When an isocyanide is hydrolyzed, an amide and formic acid are formed :



EXPERIMENT. *Isocyanide reaction.* Mix together in a test-tube a few drops of chloroform, 1 c.c. of aniline, and 2 c.c. of alcoholic KOH. Warm gently. Note the peculiar disagreeable odour of the isocyanide. As soon as detected dilute the mixture with much water in the sink, since the fumes are poisonous.

Other Cyan-compounds.

Cyanic acid may be $\text{HO}-\text{C}\equiv\text{N}$ or $\text{HN}=\text{C}=\text{O}$, or a mixture of both.

Sulphocyanic (thiocyanic) acid has sulphur replacing O in the cyanic acid molecule.

Cyan-acids, such as cyan-acetic acid, $\text{CH}_2\text{CN} \cdot \text{COOH}$, are analogous to monochloroacetic acid. Such an acid is much stronger than the simple acid and even stronger than the corresponding monochloro acid.

Substituted Ammonias. These may be considered as ammonia in which one or more hydrogen atoms are replaced by organic groups. *Primary substituted am-*

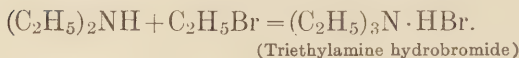
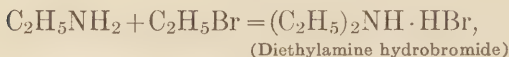
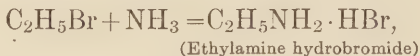
monias, $\text{N} \begin{array}{l} \text{H} \\ \diagup \quad \diagdown \\ \text{H} \end{array}$, contain the group NH_2 , called the

amido or amino group. *Secondary substituted am-*

monias, $\text{N} \begin{array}{l} \text{H} \\ \diagup \quad \diagdown \\ \text{R} \end{array}$, contain the imido group, NH . *Tertiary*

substituted ammonias, $\text{N} \begin{array}{l} \text{R} \\ \diagup \quad \diagdown \\ \text{R} \end{array}$, have all the hydrogen of ammonia displaced.

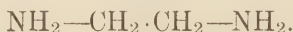
These are all called **amines**. They are prepared by the action of ammonia on alkyl halides:



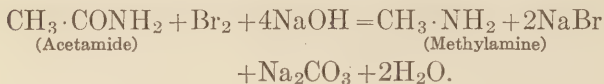
The HBr is removed by treating the above compounds with KOH.

Amines form salts with acids by adding on the entire acid molecule, N changing its valence from three to five. The salts of alkaloids are of similar nature.

Some amines have two NH_2 groups, as ethylene diamine,



The amines may also be prepared by treating an acid amide with sodium hypobromite (see exp.):

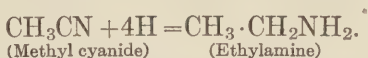


(Br forms hypobromite with NaOH.)

EXPERIMENT. Treat 12.5 gm. of dry acetamide in a half-litre flask with 11.5 c.c. of bromine; add a cooled solution of 20 gm. of KOH in 175 c.c. of water until the mixture turns a bright yellow, meanwhile keeping the flask cooled with running water. Run this hypobromite mixture by means of a dropping funnel rapidly

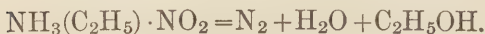
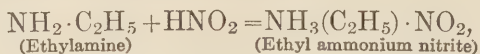
into a solution of 40 gm. of KOH in 75 c.c. of water. Keep the temperature of the liquid at 70°–75°. Cool the flask if the temperature gets above 75°. Keep at 75° for thirty minutes. Add some powdered pumice and distil on a sand bath. Attach an adapter (see fig. 19, p. 103) to the condenser; dip this slightly below the surface of strong hydrochloric acid in the receiving flask (50 c.c. C.P. HCl + 50 c.c. of water). Distil until the distillate, tested by detaching the adapter momentarily, is no longer strongly alkaline to litmus. Evaporate the acidulated distillate in an evaporating dish heated over wire gauze. When down to small bulk complete the drying in an oven at 110°. Pulverize the residue; treat with several portions of 10 c.c. of hot alcohol, filtering the decanted alcohol into a dry beaker. Crystals of methylamine hydrochloride separate out by cooling. Filter off the crystals; press between filter-paper; keep part as a specimen. Put the rest into a small test-tube, add strong KOH solution; methylamine is evolved. Note the odour and the reaction of the gas to litmus. Test its inflammability by corking the test-tube with a cork fitted with a glass tube which has a finely drawn tip, and applying a flame to this tip. Heat the mixture if necessary to secure free evolution of gas.

Nascent hydrogen converts an alkyl cyanide into an amine,



Many amines, particularly the primary ammonia bases, are decomposed by nitrous acid. This is a reaction of considerable importance. An ammonium nitrite

derivative is formed first, but this is so unstable that it breaks down, liberating nitrogen:



Many amines result from decomposition of protein material. Amines resemble ammonia in odour, and their vapours are alkaline to litmus. When dissolved in water they form bases, i.e., they give rise to hydroxyl ions. Many of the amines are more strongly basic than ammonium hydroxide.

There are **quaternary bases** in which four organic groups are linked to nitrogen; these are really substituted ammonium compounds. *Tetraethyl ammonium hydroxide* is $(\text{C}_2\text{H}_5)_4\text{NOH}$ (cf. NH_4OH). This is a very strong base; its saponifying power is almost equal to that of sodium hydroxide. If the saponifying power (*affinity constant*) of LiOH be taken as 100,

$$\text{KOH and NaOH} = 98$$

$$(\text{C}_2\text{H}_5)_4\text{NOH} = 79$$

$$\text{NH}_4\text{OH} = 2$$

Methylamine, dimethylamine, and trimethylamine are gases. They are contained in herring-brine. They are also obtained by destructive distillation of the residue which is left after preparing alcohol from the molasses of beet sugar. HCl is used to hold the amines as salts. This amine distillate is used commercially to produce methyl chloride, because the latter can be

obtained from trimethylamine by treatment with hydrochloric acid:

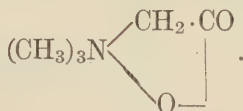


Choline is a substituted ammonium hydroxide, trimethylhydroxyethyl ammonium hydroxide:

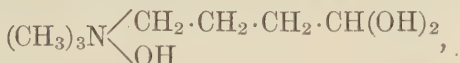


It will be noticed that it is also related to primary alcohols. It is of physiological importance.

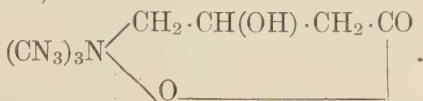
Choline is oxidized to *betaine* by removal of the H atoms of both the alcohol and the basic hydroxyl groups,



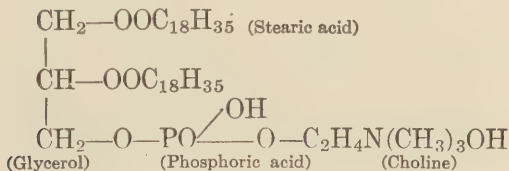
Analogous to choline and betaine are *novaine*,



and *carnitine*,



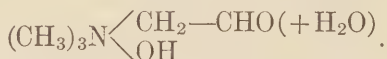
The **lecithins** are salts of choline. The principal lecithin, (distearyl lecithin) contains stearic and glycerophosphoric acids in combination with choline, having the formula



Lecithin is an important constituent of yolk of egg, of nerve-tissue, of bile, and of the envelope of red blood-corpuscles.

Phosphatides. The lecithins belong to this class of compounds. Phosphatides contain phosphoric acid in ester combination with an alcohol, generally glycerol, and one or more fatty acid radicles, and also one or more radicles containing nitrogen, generally choline. They are of importance in biochemistry. One of these is *cephalin*, which has been obtained from brain tissue. It contains the radicle of stearic acid and of an unsaturated acid of the linoleic acid series, $C_{17}H_{30}COOH$, while the nitrogenous part differs from choline in having one methyl group instead of three.

Muscarine is closely related to choline. It has been suggested that it is the aldehyde corresponding to choline considered as an alcohol:



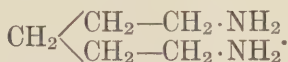
It is a basic substance classed as an alkaloid (see p. 382). Muscarine is very poisonous and is contained in toadstools (*Agaricus muscarius*) and some other plants.

Many **ptomaines**¹ are amine bases. Methylamine, dimethylamine, trimethylamine, ethylamine, diethylamine, triethylamine, propylamine, butylamine, amylamine, muscarine, and choline occur as ptomaines.

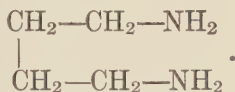
¹ Ptomaines are organic bases formed by the action of bacteria on nitrogenous matter. Decomposing animal tissue is very apt to contain ptomaines. Many of them are highly toxic and are the cause of death in certain cases of poisoning by canned meats, etc.

Cadaverine and **putrescine** are diamine ptomaines. They are highly poisonous.

Cadaverine is



Putrescine has the formula,

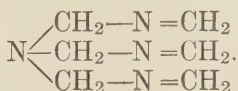


Neurine, like choline, is a ptomaine containing oxygen,

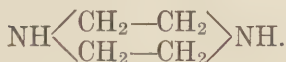


Urotropine is hexamethylentetramine, $(\text{CH}_2)_6\text{N}_4$, and is obtained by the action of ammonia on formaldehyde.

The following structural formula has been suggested,



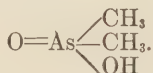
Piperazine (spermine) is diethylendiamine,



Urotropine and piperazine act as solvents for uric acid (in a test-tube at least). *Sidonal*, *lycetol*, and *lysidin* are piperazine derivatives and are used for the same purpose.

Analogous to the substituted ammonias are the substitution derivatives of phosphine (PH_3) and arsine (AsH_3). Since

they will be mentioned in no other place, it may be well in this connection to state that there are organic acids containing phosphorus or arsenic, as, for example, *cacodylic acid*, which is dimethylarsenic acid,



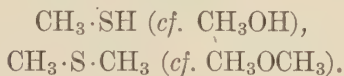
Nitro Compounds.—Nitroparaffins have N of the nitro group linked directly to C of the chain, e.g., nitroethane, $\text{CH}_3\cdot\text{CH}_2\text{—NO}_2$. The nitro compounds of the benzenes are much more important than are those of the paraffins, and will be considered later.

The Nitrites, ethyl nitrite, $\text{C}_2\text{H}_5\text{—O—NO}$, and isoamyl nitrite, $\text{C}_5\text{H}_{11}\text{—O—NO}$ are of importance. Both are used as medicines. Amyl nitrite is a very valuable remedy; its physiological action is similar to that of nitroglycerol (see p. 175), but comes on quickly and is very evanescent. These organic nitrites are often called nitrous esters, being formed by the action of nitrous acid on alcohols.

EXPERIMENT. Prepare amyl nitrite as follows: Mix in a small flask 20 c.c. of fermentation amyl alcohol and 15 gm. of finely powdered sodium nitrite. Set the flask in ice-water; add to the alcohol, drop by drop, 5 c.c. of C.P. H_2SO_4 from a dropping funnel. Amyl nitrite forms a top layer; decant it off into a separating funnel. Add some water to the mixture in the flask and shake; more amyl nitrite separates out; decant again. Separate the nitrite from the aqueous liquid. Dry with calcium chloride and distil. Note the colour, odour, and the effect of cautious inhalation (flushing of the face and vascular throbbing).

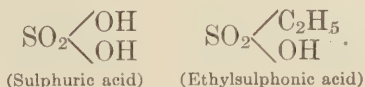
SULPHUR DERIVATIVES.

Sulphur may take the place of oxygen in alcohols or ethers, forming **sulphur alcohols** and **ethers**, as



Sulphur alcohols are called mercaptans or thioalcohols. The ethers are dialkyl sulphides. When they are oxidized, as with nitric acid, **sulphonic acids** are formed, $\text{CH}_3 \cdot \text{SH} + 3\text{O} = \text{CH}_3 \cdot \text{SO}_3\text{H}$. The sulphonic acid group is SO_3H .

Sulphonic acids may be looked upon as sulphuric acid in which an hydroxyl group is replaced by an organic group:



A *sulphone* is obtained if the hydroxyl of the SO_3H group be substituted by an organic radicle. The sulphonic acids are of more importance in the chemistry of aromatic compounds.

There are three aliphatic sulphonic derivatives of importance, because they are used as hypnotics.

Sulphonal (sulphonmethane), diethylsulphonedimethylmethane, $\begin{array}{c} \text{CH}_3 \\ \diagdown \\ \text{C} \\ \diagup \\ \text{CH}_3 \end{array} \begin{array}{l} \diagdown \text{SO}_2\text{C}_2\text{H}_5 \\ \diagup \text{SO}_2\text{C}_2\text{H}_5 \end{array}$, is made from acetone and ethyl mercaptan. It forms colourless crystals, slightly soluble in cold water, quite soluble in hot water.

Trional (sulphonethylmethane) is



Tetronal is



Ichthyol consists largely of a mixture of the ammonium salts of certain sulphonic acids derived from the tar, which is obtained by distillation of a bituminous shale (found in the Tyrol) that contains the fossil remains of fishes.

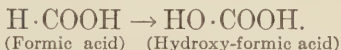
CHAPTER XVII.

MIXED COMPOUNDS. HYDROXY-ACIDS.

UNDER mixed compounds we shall consider hydroxy-acids, amido compounds, and carbohydrates.

Hydroxy-acids contain both alcohol (OH) and acid (COOH) groups. The acid properties, however, are more marked than the alcohol properties. They are not acid alcohols, but hydroxy-acids, and may therefore be defined as acids in which a hydrogen atom attached to one of the carbon atoms is replaced by hydroxyl. They are often called oxy-acids.

The simplest possible hydroxy-acid would be *hydroxy-formic acid*,



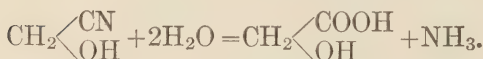
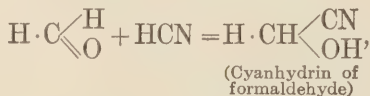
It will be observed that this is identical with the hypothetical carbonic acid, H_2CO_3 .

The lowest typical hydroxy-acid is hydroxyacetic acid, $\text{CH}_2 \begin{smallmatrix} \diagup \text{OH} \\ \diagdown \text{COOH} \end{smallmatrix}$, or glycollic acid (mentioned previously under glycol).

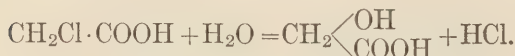
Glycollic acid (ethanolic acid) may be prepared in many ways, starting either with an alcohol or an acid:

(1) By oxidation of glycol or glycol aldehyde (see p. 168).

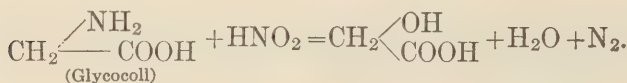
(2) By forming the cyanogen derivatives of methyl alcohol, or, what is the same thing, the cyanhydrin of formaldehyde; then hydrolyzing:



(3) By boiling monochloracetic acid with water:



(4) By treating aminoacetic acid (glycocoll) with nitrous acid:



These methods are in general applicable to other hydroxy-acids.

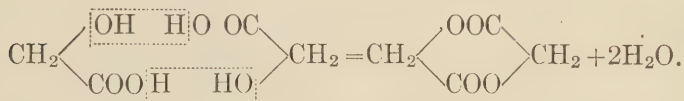
Glycollic acid (as also other hydroxy-acids) forms ethereal salts similar not only to salts of other acids, but also to salts of alcohols. There is ethyl gly-

collate,¹ $\text{CH}_2 \begin{array}{l} \diagup \text{OH} \\ \diagdown \text{COO} \cdot \text{C}_2\text{H}_5 \end{array}$, and ethyl-glycollic acid, $\text{CH}_2 \begin{array}{l} \diagup \text{OC}_2\text{H}_5 \\ \diagdown \text{COOH} \end{array}$, also glycollic acetate, $\text{CH}_2 \begin{array}{l} \diagup \text{OOC} \cdot \text{CH}_3 \\ \diagdown \text{COOH} \end{array}$.

Glycollic acid is found in green grapes and elsewhere.

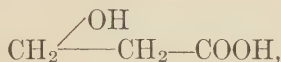
¹ Distinguish glycollates from the glycolates derived from glycol (p. 168).

It forms needle crystals, melting at 80° . It is a stronger acid than acetic acid. When heated in an atmosphere of carbon dioxide at 210° it combines with itself, losing water, thus forming an anhydride called *glycollid*:



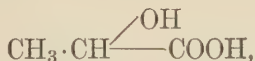
This has neither alcoholic nor acidic properties.

Hydroxypropionic acids are commonly called **lactic acids**. Just as there are two monochloropropionic acids, α and β , so there is an α -hydroxypropionic acid and a β -hydroxypropionic acid. The β acid,



shows by its reactions that it is related to ethylene (see p. 269). It is therefore called ethylene lactic acid. It is unimportant.

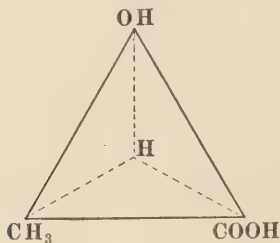
Lactic acid proper, α -hydroxypropionic acid,



is known in three forms as isomers. As with some of the amyl alcohols (p. 120), these isomers have identical structural formulæ. Isomerism of the kind to be described now is called *stereoisomerism*.¹ To understand

¹ Stereochemistry (*stereos* meaning solid) treats of those chemical and physical phenomena that are supposed to be caused by the relative positions in space that are occupied by the atoms within the molecule.

this it is necessary to conceive of the atoms of the molecules as being arranged in space, and not on one plane as in ordinary formulæ. The main carbon atom is thought of as being placed in the centre of a tetrahedron, at the apex of each solid angle of which is situated an atom or group. Models of wood or pasteboard will be helpful in understanding this. To represent α -lactic acid, write the groups CH_3 , OH , H , and COOH at the corners of the tetrahedron, thus:

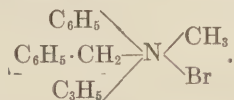


Try the effect of interchanging these groups in all possible ways. It will be found that two and only two different arrangements are possible.¹ Further, by holding the tetrahedron representing one combination before a mirror, the image in the mirror will be seen to correspond exactly to the other possible arrangement. This is true only in the case of compounds which would be represented as having four *different* groups at the corners. If two of these groups are the same, only one arrangement is possible and stereoisomerism cannot occur.

¹ The truth of this statement can be most clearly shown by writing down the various possible arrangements and then marking off those that are identical.

The tetrahedron representing lactic acid is unsymmetrical as regards the kind of groups present; its central carbon atom is therefore said to be an *asymmetric* carbon atom. It has been found that compounds containing an asymmetric carbon atom rotate the plane of polarized light.¹ Dextrolactic acid rotates it to the right, lævolactic acid rotates it to the left. As represented by models lævolactic acid is the mirror-image of dextrolactic acid. Ordinary lactic is also an α -lactic acid, but it does not affect polarized light; it is optically inactive. It has been shown to consist of equal quantities of dextrolactic and lævolactic acid molecules; such a substance is called *racemic*.² The two constituent acids of racemic acid neutralize each other in their action on polarized light. Optically active substances that have a physiological action may show a different degree of action on the animal organism according to whether it is the *d* or *l* isomer that is acting (see nicotine, p. 386, atropine, p. 388, and cocaine, p. 390).

¹ A few optically active organic compounds have been prepared which contain asymmetric atoms other than carbon. Certain quaternary bases have an asymmetric N atom, as



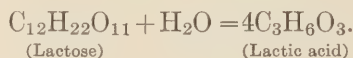
The pentavalent N atom has been conceived of as at the centre of a pyramid.

² Racemic substances are not always mixtures; the mixtures might better be called *conglomerates*. The racemic, properly speaking, contain the two active molecules in some sort of molecular combination (*cf.* tartaric acid).

Dextrolactic acid (*d*-lactic acid) is also called *sarc-lactic acid*, because it occurs in flesh. It is present in beef extract. It is also the product of fermentation of dextrose by the *Micrococcus acidi paralactici*. Its salts are lævorotatory.

Lævolactic acid (*l*-lactic acid) is obtainable by fermentation of dextrose by the *Micrococcus acidi lævolactici*.

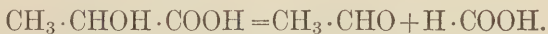
Racemic lactic acid (*d*-, *l*-lactic acid) is a syrupy liquid having a specific gravity of 1.2485 at $\frac{15^{\circ}}{4^{\circ}}$. It is stronger than most organic acids. This is much stronger than propionic and ethylene lactic acids, to which it is related. It is the product of ordinary lactic acid fermentation. When milk sours, milk-sugar becomes converted into lactic acid by microorganisms:



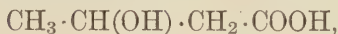
No matter in what way lactic acid is artificially produced by synthesis, the synthetic acid is always racemic. The law of probability as applied to chemical synthesis calls for the formation of just as many molecules having the dextro-arrangement as the lævo. *d*, *l*-Lactic acid can be shown to contain dextrolactic acid by growing the mould *Penicillium glaucum* in a solution of *d*, *l*-ammonium lactate: the mould destroys the lævolactic acid. It may be shown to contain lævolactic acid by fractional crystallization of a solution of strychnine lactate, inasmuch as the lævolactate crystals are formed first.

When heated to 150° in dry air lactic acid changes to an anhydride called lactid (*cf.* glycollic acid, p. 198). Hydriodic acid reduces lactic acid to propionic acid (see p. 159).

EXPERIMENT. In a retort mix 5 c.c. of lactic acid, 10 c.c. of water, and 5 c.c. of concentrated H_2SO_4 . Connect with a condenser. Heat with a smoky flame. Test the distillate for aldehyde (see p. 129) and for formic acid (see p. 137):

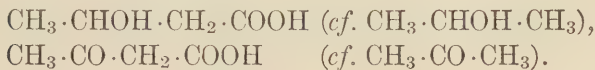


β -Hydroxybutyric acid (β -oxybutyric acid),



is pathologically of importance, since it may occur in blood or urine, especially in the disease diabetes. It is lævorotatory, its specific rotation (p. 260) being -24.12° .

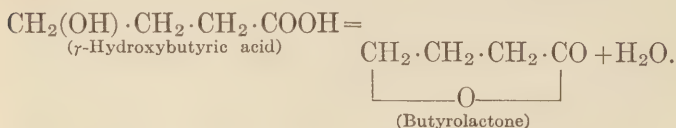
It will be noticed that the ketone acid *acetoacetic acid* (β -ketobutyric acid) corresponds to the above alcohol acids, just as ketones correspond to secondary alcohols (see also p. 166):



β -hydroxybutyric acid can be readily oxidized to acetoacetic acid by hydrogen peroxide.

β -Hydroxyethylsulphonic acid (isethionic acid), $\text{CH}_2(\text{OH}) \cdot \text{CH}_2 \cdot \text{SO}_3\text{H}$, enters into the synthesis of taurin (see p. 217).

γ -Hydroxy-acids are very unstable. They readily split off water to form anhydrides called **lactones**, thus:



The carbon chain is closed by a linking through oxygen. It is not a typical closed chain, however. The presence of hydrogen ions acts catalytically to hasten the formation of the lactone, and it is supposed that the H ions of γ -hydroxy acid itself have this action, causing *autocatalysis*. When boiled with caustic alkalis the lactones form salts of the corresponding hydroxy-acids; thus lactones give a "saponification value." This fact must be borne in mind in examining unknown substances supposed to be fats or waxes.

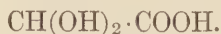
Dihydroxy-monobasic acids are illustrated by **glyceric acid**,



Glyoxylic acid, which has been previously mentioned (p. 168), while classed as an aldehydic acid, is really a dihydroxy-acid, because it holds a molecule of water inseparable from it (*cf.* chloral hydrate):

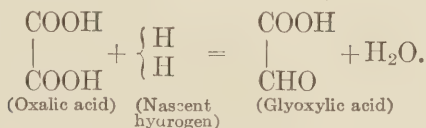


or



It is a reducing agent like aldehydes (as chloral hydrate).

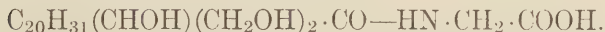
EXPERIMENTS. (1) To 20 c.c. of a strong solution of oxalic acid add 1 gm. sodium amalgam; when evolution of gas has ceased, filter. The filtrate is a dilute solution of glyoxylic acid:



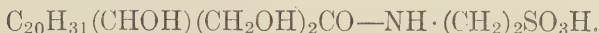
(2) To 5 c.c. of albumin solution (egg-white solution) add 5 c.c. of the glyoxylic acid solution, then 5 c.c. of concentrated H_2SO_4 ; mix and heat gradually; a bluish-violet color is obtained, due to tryptophan contained in the protein molecule. Most proteins give this test.

An example of a **trihydroxy-acid** is **cholic** or cholalic acid, $\text{C}_{20}\text{H}_{31}(\text{CHOH}) \cdot (\text{CH}_2\text{OH})_2 \cdot \text{COOH}$. The constitution of the $\text{C}_{20}\text{H}_{31}$ portion of the formula is unknown. This is important physiologically, being contained, in combination with glycine and with taurine, in bile.

Glycocholic acid has the formula:



Taurocholic acid is



Glycuronic acid is an **aldehydic tetrahydroxy-acid**, $\text{CHO} \cdot (\text{CHOH})_4 \cdot \text{COOH}$, the arrangement of the secondary alcohol groups being the same as in dextrose. It is formed by the animal body from dextrose when it

is needed to combine with abnormal substances, as drugs or indol (when there is an insufficiency of SO_4 , see p. 375). It is excreted in the urine as *paired glycuronates*; these are lævorotatory. By heating with dilute acid, glycuronic acid is set free; this is dextro-rotatory. It is closely related to monosaccharides, differing only in the change of the CH_2OH group to COOH . The free acid and some of its combinations reduce alkaline copper solutions (like other aldehydes), more particularly after prolonged heating of the mixture. This may cause a mistake in urine examination. It is not fermentable. It gives the pentose reactions (see p. 245).

Monohydroxydibasic Acids.

Tartronic acid, $\begin{array}{c} \text{COOH} \\ | \\ \text{CHOH} \\ | \\ \text{COOH} \end{array}$, has been supposed to take part in the physiological synthesis of uric acid, particularly in birds (see p. 234).

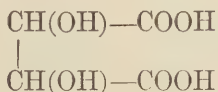
Malic acid is hydroxysuccinic acid, $\begin{array}{c} \text{CH(OH)—COOH} \\ | \\ \text{CH}_2\text{—COOH} \end{array}$. It is contained in sour fruits, e.g., apples and cherries.

Dihydroxydibasic Acids.

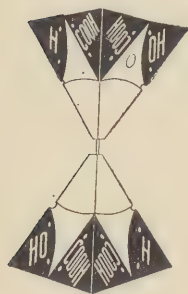
Mesoxalic acid, $\begin{array}{c} \text{COOH} \\ | \quad \text{OH} \\ \text{C} \diagup \quad \diagdown \\ | \quad \text{OH} \\ \text{COOH} \end{array}$, is the third exception to the

rule that two hydroxyls cannot be attached to the same carbon atom, chloral hydrate and glyoxylic acid being the other two exceptions.

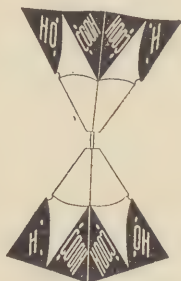
Tartaric acid is dihydroxysuccinic acid,



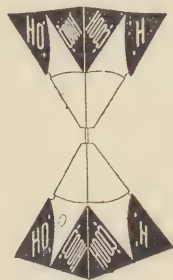
Here there are *two* asymmetric carbon atoms (see p. 199) in the molecule. This fact causes a species of stereoisomerism which is more difficult to understand than that of lactic acid. With the aid of models it can be clearly understood. Arrange pairs of tetrahedra as shown in the diagram.



Dextro-tartaric acid.



Laevo-tartaric acid.



Meso-tartaric acid.

FIG. 22.

It will be noticed in the case of *dextro*- and *laevo*-tartaric acids that the groups, OH and OH, H and H, are connected by straight lines and are on opposite sides of a line connecting the centres of the tetrahedra; they are diagonally opposite, while the COOH groups are vertically opposite one another, both being at an angle

of the tetrahedron which points forward. As with the models for lactic acid, these models for active tartaric acids cannot be made identical by turning the model about.

Place the lævotartaric model before a mirror; the image corresponds to dextrotartaric acid.

Racemic tartaric acid when in solution is a mixture of equal quantities of dextro- and lævo-tartaric acids (*cf.* racemic lactic acid)¹. There is, however, another inactive tartaric acid which cannot be separated into optically active acids. This is *mesotartaric acid*. By studying the diagram above, or a model, it will be seen that the neutralization of optical properties is an inner molecular one, for the arrangement of the groups on the top corresponds to that of lævotartaric acid, while the arrangement at the base corresponds to that of dextrotartaric.²

Racemic and mesotartaric acids differ widely in melting-point and solubility.

Ordinary tartaric acid is dextrorotatory. It is contained in grape-juice as potassium bitartrate or acid tartrate, $\text{HOOC}(\text{CHOH})_2\text{COOK}$. When wine is produced this salt separates out, because of its relative insolubility in dilute alcohol. This crude tartar, or argol, is called cream of tartar when purified. It is used in the manufacture of the best baking-powders. Baking-powder is a mixture of sodium bicarbonate and some acid salt, which on being dissolved liberates car-

¹ The racemic tartaric acid *crystals*, however, are represented by the formula $4\text{C}_4\text{H}_6\text{O}_6 + 2\text{H}_2\text{O}$.

² It will further be noted that an acid of this variety is not possible in the case of lactic acid.

bon dioxide from the bicarbonate. Tartaric acid is obtained from potassium bitartrate by precipitation of calcium tartrate, from which the acid is liberated by using the proper amount of dilute sulphuric acid. It forms large crystals, melting at 170° . On heating further it turns brown and gives off an odour like caramel. It is very soluble.

Dextrotartaric acid can be converted into racemic acid by boiling with an excess of strong sodium hydroxide solution. The two methods given for separating racemic lactic acid into the active acids are applicable also to racemic tartaric acid. Pasteur discovered a third method which is very interesting. By slow evaporation (below 28°) of a solution of sodium ammonium racemate two classes of crystals can be obtained, which from their appearance might be called right-handed and left-handed crystals (see Fig. 23).

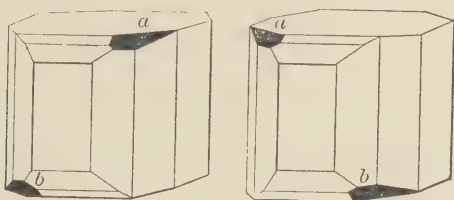
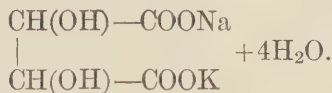


FIG. 23.

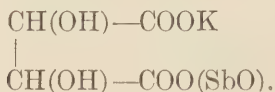
The crystals are mirror-images of one another. These can be picked out mechanically; one set furnishes dextrotartaric acid, the other lævotartaric acid.

Rochelle salts is sodium potassium tartrate,



This has the power of holding $\text{Cu}(\text{OH})_2$ in solution. as in Fehling's solution. It is used as a cathartic.

Tartar emetic is potassium antimonyl tartrate,



It is used as a medicine.

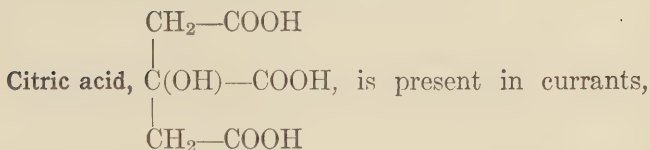
EXPERIMENTS. (1) Heat some tartaric acid in a test-tube, stirring it with a thermometer. Note the melting-point. Remove the thermometer and continue heating. The acid turns brown and emits an odour like scorched sugar.¹

(2) Prepare tartar emetic. Dissolve 5 gm. of potassium acid tartrate in 50 c.c. of water, add 4 gm. Sb_2O_3 and boil. Filter and test some of the filtrate for antimony with H_2S . Set aside the rest of the filtrate to secure crystals by slow evaporation.

(3) After reading over a description of the polariscope² and its manipulation, determine the rotary power of a strong solution of tartaric acid.

¹ Certain other acids act in the same way, particularly citric, malic, tannic, and gallic.

² A good description can be found in *Cohen's Practical Organic Chemistry*, also in *Practical Physiology* by *Beddard, Macleod*, etc.

Monohydroxytribasic Acids.

gooseberries, and lemons. It forms large crystals and is quite soluble. Citrates are valuable medicines (diuretics).

Agaric or **agaricinic acid** is used as a remedy. Its formula is $\text{C}_{19}\text{H}_{36}(\text{OH})(\text{COOH})_3$. Other hydroxyacids that are mentioned elsewhere are dihydroxystearic acid (p. 179) and ricinoleic acid (p. 272).

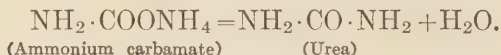
CHAPTER XVIII.

MIXED COMPOUNDS (*Continued*). AMIDO ACIDS AND ACID AMIDES.

AMIDO ACIDS.

Amido or **am'no acids** are acids containing an NH_2 or amido group. Corresponding to monochloracetic acid, $\text{CH}_2\text{Cl}\cdot\text{COOH}$, is aminoacetic acid, $\text{CH}_2\text{NH}_2\cdot\text{COOH}$.

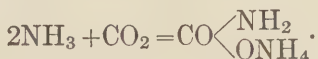
The simplest amino acid is aminoformic acid, $\text{NH}_2\cdot\text{COOH}$, called **carbamic acid**. The free acid is unknown. The salts are unstable, showing a decided tendency to become converted into carbonates. Ammonium carbamate is of considerable importance in physiology, because it is believed to be one of the forerunners of urea. It can be changed into urea by heating it in a sealed tube at a temperature of 135° – 140° :



EXPERIMENT. Prepare ammonium carbamate by bubbling dry CO_2 ¹ and dry NH_3 simultaneously into alcohol contained in a cylinder or graduate. Secure the

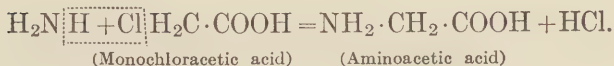
¹ CO_2 is obtained by putting marble chips into a bottle or generator and adding HCl by a dropping funnel.

dry NH_3 as previously described (see p. 129). Dry the CO_2 by bubbling it through H_2SO_4 . When a considerable quantity of crystals has been produced, stop the process. Filter off the alcohol; press the crystals between filter-paper. To test the carbamate, dissolve some of the crystals in 5 c.c. of distilled water which has been cooled to 0° ; immediately add some CaCl_2 solution which has been similarly cooled. No reaction is apparent because calcium carbamate in solution is stable at very low temperatures. Now warm the solution; the carbamate decomposes and a heavy precipitate of calcium carbonate appears. Leave the rest of the crystals exposed to the air several days; a small amount of a white powder (NH_4HCO_3) is obtained:



Ethyl carbamate, or **urethane**, $\text{NH}_2 \cdot \text{COOC}_2\text{H}_5$, is used as a hypnotic.

Amino acids may be obtained by treating a halogen fatty acid with ammonia, thus:



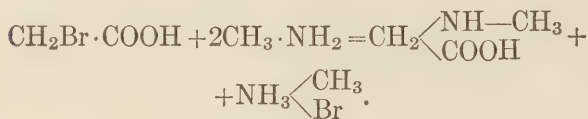
Ammonium salts are, of course, formed. They can also be obtained by decomposing proteins by means of acids, alkalies, or hydrolytic ferments.

All the amino-acids that are considered in this chapter

are of great importance in physiology. They are very weak acids. In fact they are amphoteric electrolytes, their solutions behaving as if they contained both hydrogen and hydroxyl ions. The amino group gives the basic character to the molecule. Proteins and some other organic compounds act in the same manner.

Glycocoll (glycin) is aminoacetic acid, $\text{CH}_2\text{—}\begin{smallmatrix} \text{NH}_2 \\ \diagup \end{smallmatrix}\text{COOH}$. It can be produced from glue (or gelatin) by boiling with dilute sulphuric acid or baryta water. It can be prepared by allowing an excess of strong ammonium hydroxide to act on monochloracetic acid for 24 hours. In the animal body it combines with benzoic acid to form hippuric acid (see p. 322), and with cholic acid to form one of the bile acids, glycocholic acid.

Methyl glycocoll, $\text{CH}_2\text{—}\begin{smallmatrix} \text{NH}\cdot\text{CH}_3 \\ \diagup \end{smallmatrix}\text{COOH}$, is called *sarcosin*. It can be synthesized from monobromacetic acid and methylamine:



It is a product of decomposition of creatin and of caffeine.

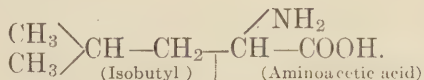
Alanin, $\text{CH}_3\cdot\text{CH}\cdot\text{NH}_2\cdot\text{COOH}$, is α -aminopropionic acid. It can be made from α -chlorpropionic acid by treatment with ammonia. It is isomeric with sarcosin.

Serin is hydroxyalanin, $\cdot\text{CH}_2\text{OH}\cdot\text{CHNH}_2\cdot\text{COOH}$.

Valin is α -aminoisovaleric acid,



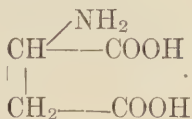
Leucin is α -aminoisobutylacetic acid, or α -amino-isocaproic acid,



This may occur in the urine in certain diseases. It is a decomposition product of protein, being an important end product of tryptic digestion.

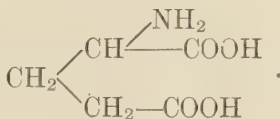
Isoleucin, $\begin{array}{c} \text{C}_2\text{H}_5 \\ \text{CH}_3 \end{array} \begin{array}{l} \diagup \\ \diagdown \end{array} \text{CH} - \text{CH} \begin{array}{l} \diagup \text{NH}_2 \\ \diagdown \text{COOH} \end{array}$ is contained in certain proteins.

Aspartic acid (asparaginic acid) is aminosuccinic acid,



It is obtainable from asparagin and from protein.

Glutaminic acid (glutamic acid) is α -aminoglutaric acid,

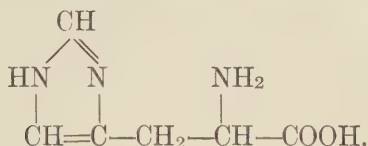


Gelatin and caseinogen can be split up so as to furnish a considerable proportion of this acid.

Phenylalanin and **tyrosin** are aromatic mono-amino-acids derived from proteins (see p. 353). The amino

A ferment, arginase, found mainly in the liver, can also bring about this hydrolysis.

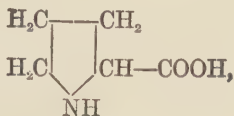
Lysin and arginin are called **hexone bases** (hexone refers to their possessing six carbon atoms in the molecule). Another hexone base is **histidin**, $C_6H_9N_3O_2$, probably β -imidazol α -aminopropionic acid,



It is a heterocyclic compound. (See p. 373.) It is now believed that these hexone bases are present in combination in all protein molecules. The simplest proteins, *protamines*, seem to contain practically nothing besides hexone bases.

Another heterocyclic compound derived from proteins is **tryptophan** (see p. 376), also an α -amino acid.

It seems advisable to mention in this place two derivatives of pyrrolidine (a heterocyclic compound, p. 373), because they are obtained together with the above amino acids as decomposition products of proteins. They are *prolin* or α -pyrrolidine-carboxylic acid,



and γ -hydroxy- α -pyrrolidine-carboxylic acid or *hydroxyprolin*.

Optical activity of the decomposition products of proteins. Alanin, valin, isoleucin, glutaminic acid, ornithin, arginin and lysin are dextrorotatory. Serin, leucin,

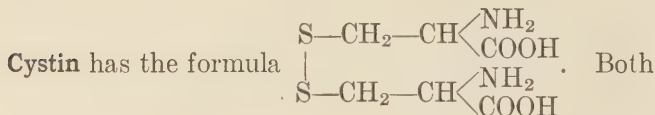
cystin, aspartic acid, histidin, phenylalanin, tyrosin, tryptophan, prolin and hydroxyprolin are lævorotatory.

SULPHUR DERIVATIVES OF AMINO ACIDS.

Cystein is α -amino- β -thiolactic acid:



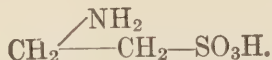
Two molecules combine to form one molecule of cystin.



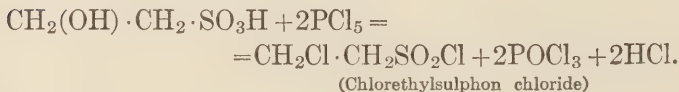
cystein and cystin occur as decomposition products of proteins.

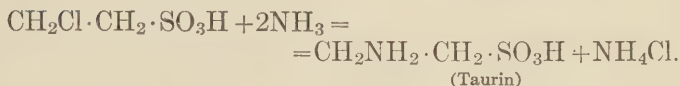
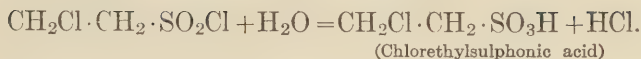
Cystin crystals may occur in pathological urine. Reduction of cystin gives cystein as its product.

Taurin is β -aminoethylsulphonic acid,



It is found in bile combined with cholic acid as taurocholic acid. It has been synthesized from β -hydroxyethylsulphonic acid (see p. 202), as indicated by the following equations:



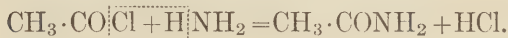


ACID AMIDES.

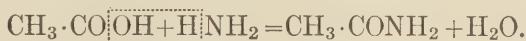
The next group of amido compounds to be considered is that of the acid amides. Just as there are acid chlorides, e.g., acetyl chloride, $\text{CH}_3 \cdot \text{COCl}$, so there are acid amides, NH_2 occupying the position of Cl , as acetamide, $\text{CH}_3 \cdot \text{CONH}_2$.

Acid amides may be made in several ways:

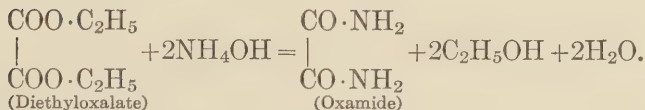
(1) By treating an acid chloride with ammonia:



(2) By heating an acid in an atmosphere of ammonia while constantly bubbling dry ammonia gas into the acid:

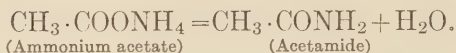


(3) By treating an ester with ammonia:



(4) By heating the ammonium salt of the acid, gener-

ally in a sealed tube (the process being anhydrol-
ysis).



Acid amides are decomposed by the action of nitrous acid, nitrogen being liberated. Amides are hydrolyzed by water, the action being greatly accelerated by hydrogen ions. This can be taken advantage of to determine hydron concentration of solutions of different acids (p. 148 and appendix). The simpler amides, as formamide, conduct electricity. Solution of salts in these ionize somewhat.

Formamide, $\text{H} \cdot \text{CONH}_2$, is a liquid. The other acid amides are solid crystalline substances.

Acetamide, $\text{CH}_3 \cdot \text{CONH}_2$, is prepared by the fourth method given above (see exp.). It can also be prepared by the action of ammonium hydroxide on ethyl acetate. It forms colourless crystals, which melt at 82° and distil at 223° . It generally has a mouse-like odour, due to slight admixture of impurities. It can be purified by crystallization from chloroform. Heating with phosphorus pentoxide converts it into methyl cyanide (see p. 184).

EXPERIMENT. To 40 gm. of glacial acetic acid heated in an evaporating dish to 40° – 50° on a water bath, add powdered ammonium carbonate (about 55 gm.) while stirring until a drop diluted with a few cubic centimeters of water shows a weak alkaline reaction to litmus. Now heat to 80° – 90° on a boiling water bath until a drop diluted with water shows a slightly acid reaction. Pour the mass while hot into a Volhard

tube or bomb-tube through a hot funnel (so as not to smear the walls of the tube). With a strip of filter-paper remove any of the substance that may be adhering to the upper eight inches of the tube.

Seal the tube carefully. The sealing of bomb-tubes requires practice. Experiment first with waste pieces of tubing. First cover the tube with soot in a smoky flame at the point where it is to be sealed. Increase the heat gradually, then begin with a large blast flame. When the soot is burned off, decrease the size of the flame, increasing the force of the blast. Keep rotating the tube, and when it softens do not draw it out, but make the tube sink in by the force of the blast. In this way the thickness of the wall is preserved. When the calibre of the tube has become very small, the tube can be quickly drawn out and sealed off. A tapering tip is the best. Heat the tip in the flame until rounded. Keep the hot end of the tube in a cold smoky flame until a deposit of soot is obtained. Let it cool slowly.

Heat the tube in a bomb-furnace for five hours at 220° – 230° . Open the tube by making a scratch-mark with a file on the tip; wrap the tube in a heavy towel; put the tip into the blast-flame, when it will snap off. Sometimes there is a high pressure of gases in a bomb-tube, so that it may fly to pieces as soon as the pressure is suddenly relieved. Break off the end of the tube; remove the acetamide and transfer it to a distilling flask. Distil, reject the distillate coming over below 130° , then change to a wide tube (air-condenser) in the place of the Liebig condenser. Collect the fraction distilling between 180° and 230° in a beaker. Cool it with ice-water until crystals form; if necessary, scratch the wall of the beaker with the sharp end of a glass rod

(see p. 8). Dry the crystals by pressing them on a porous plate.

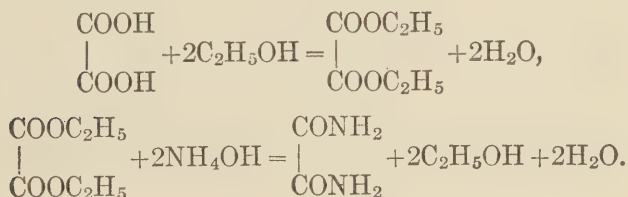
An easier method of preparation of acetamide is as follows: Let a mixture of 50 gm. of ethyl acetate and 100 c.c. of concentrated ammonium hydroxide stand for one week. Distil as above.

Glycinamide, $\text{NH}_2 \cdot \text{CH}_2 \cdot \text{CONH}_2$, the acid amide of glycocoll, is of interest in connection with the biuret test (pp. 226, and 241).

Oxamide, $\begin{array}{c} \text{CONH}_2 \\ | \\ \text{CONH}_2 \end{array}$, is prepared by the third method.

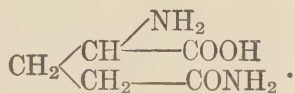
EXPERIMENT. Connect two flasks with a glass tube bent at a right angle at each end. In the second flask the tube is long enough to almost reach the bottom. Into each flask put 50 c.c. of alcohol. Into the second flask put also 50 gm. of oxalic acid from which the water of crystallization has been driven off by heating in an oven at 100° . The first flask is supported on wire gauze, while the second is placed in an oil-bath. Place a thermometer in the oil. Connect the second flask with a condenser. Heat the oil-bath to 100° , then begin heating the flask containing only alcohol. While the alcohol-vapour is passing over, allow the temperature of the oil-bath to rise slowly to 125° – 130° . When most of the alcohol has disappeared from flask number one, disconnect this flask and remove the flame. The distillate and the residue in flask number two both contain diethyl oxalate. Treat each with strong ammonium hydroxide. A white precipitate of oxamide is obtained. Filter and wash the

precipitate thoroughly. Save a sample. Put some oxamide into a test-tube, add strong alkali, and boil, noting the evolution of ammonia. Take another portion in a test-tube, treat with cold NaOH, and add very dilute copper sulphate solution a drop at a time until a reddish or violet colour appears (biuret reaction, see p. 226):



Asparagin is the mono-amide of aspartic acid, its formula being $\begin{array}{c} \text{CH}_2\text{—CONH}_2 \\ | \\ \text{CH(NH}_2\text{)—COOH} \end{array}$. It occurs both as the dextro and lævo variety; the commoner kind (lævo) is tasteless while the dextro tastes sweet. It is found in many vegetables, particularly asparagus, peas, beans, beets, and wheat.

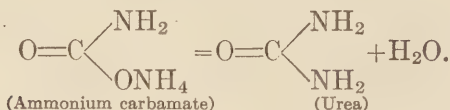
Glutamin is the mono-amide of glutaminic acid, having the formula



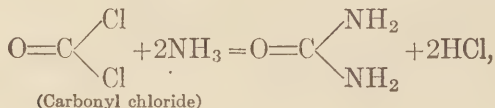
The most important acid amide of all is *carbamide*. **Urea** (carbamide), $\text{NH}_2\cdot\text{CONH}_2$, is the acid amide of carbamic acid. It is also the diamide of carbonic acid:



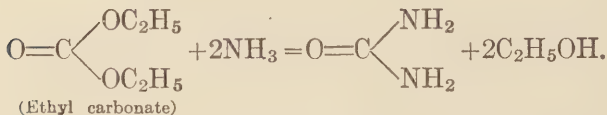
The relationship of urea to carbamic acid is shown by its preparation from ammonium carbamate by heating in a sealed tube at a temperature of 135° :



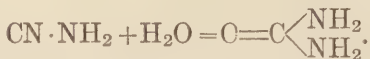
Its relationship to carbonic acid is evidenced by its production from carbonyl chloride and ammonia:



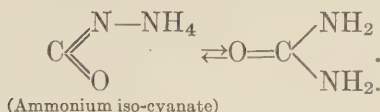
also from ethyl carbonate and ammonia:



That it bears a relationship to cyanic acid, HCNO , and its amide cyanamide, $\text{N}\equiv\text{C}-\text{NH}_2$, is proven by its preparation from both of these. By hydrolysis cyanamide is converted into urea:

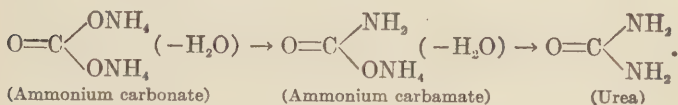


Mere evaporation of a solution of ammonium isocyanate is sufficient to convert the salt into urea (see exp.); this involves intramolecular change:



The change of cyanate to urea is a reversible reaction. A decinormal solution of ammonium isocyanate changes on standing until it reaches an equilibrium point, at which 95 per cent of the cyanate has become urea. On the other hand a urea solution changes until it reaches the same equilibrium point, i.e., when 5 per cent has been changed to cyanate.

Physiologists have advocated three main hypotheses as to the origin of urea in the animal body, corresponding to the above methods of synthesis, namely, that it is derived from (1) ammonium carbonate, (2) from ammonium carbamate, or (3) from ammonium cyanate. It seems most likely that the derivation of urea is as follows: Ammonia enters the blood of the portal venous system mainly as the result of fermentative and bacterial hydrolysis of the proteins of the food. In the presence of the large amount of carbonic acid in the blood, ammonium carbonate and carbamate are formed in accordance with the laws of mass action; both of these are then converted in the liver into urea by a process of anhydrolysis:

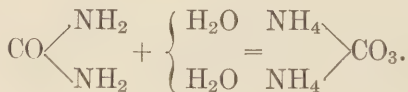


General tissue metabolism probably gives rise to monoamino-acids (as glycocoll, leucin, and aspartic acid) and arginin, all of which are convertible into urea (at least as a laboratory

experiment). In the case of arginin this is accomplished by a ferment, arginase, which is present in many organs. In the case of monoamino-acids it may be that they are converted by ferments (deamidation) into ammonia, for the presence of ferments possessing that power has been demonstrated in many organs, and that then the ammonia becomes ammonium carbonate and carbamate, and is changed to urea.

Urine contains a large quantity of urea, 20 to 30 gm. of urea being excreted in the urine of man in twenty-four hours on a mixed diet. It crystallizes in colourless needles or rhombic prisms. It melts at 132° (corrected melting-point is 132.6°). It is very soluble in water and hot alcohol, less soluble in cold alcohol.

Bacterial fermentation of urine converts urea into ammonium carbonate, hence the ammoniacal odour of decomposed urine. Boiling with alkalies or acids or superheating with water accomplishes a similar hydrolysis:

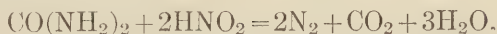


Of course by the action of alkali NH_3 is liberated from the $(\text{NH}_4)_2\text{CO}_3$, while by the action of acid CO_2 is liberated. This reaction is the basis of Bunsen's and Folin's methods of quantitative estimation of urea. Sodium hypochlorite and hypobromite decompose urea, liberating nitrogen:



This reaction is made use of in the usual clinical method

for urea estimation. Nitrous acid also liberates free nitrogen (see p. 189):



When heated strongly, urea yields, among other substances, *biuret*, $\text{NH}_2 \cdot \text{CO} \cdot \text{NH} \cdot \text{CO} \cdot \text{NH}_2$, which gives a reddish-violet colour reaction with caustic soda or potash containing a trace of copper sulphate (*biuret reaction*). This reaction is given by proteins, by oxamide, in fact by all substances containing two groups of $\text{CO} \cdot \text{NH}_2$ linked together either directly (as in oxamide) or through a single nitrogen (as in biuret) or carbon atom

(as in $\text{CH}_2 \begin{smallmatrix} \text{CONH}_2 \\ \diagdown \\ \text{CONH}_2 \end{smallmatrix}$), or through one or more $\text{CO} \cdot \text{NH}$ groups $\left(\text{as in } \begin{smallmatrix} \text{CO} \cdot \text{CONH}_2 \\ | \\ \text{NH} \cdot \text{CONH}_2 \end{smallmatrix} \right)$.

$\text{CH}_2 \cdot \text{NH}_2$ may take the place of one of the CONH_2 groups, as in glycineamide (pp. 221 and 241).

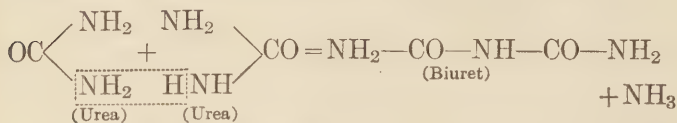
Urea acts as a weak monacid base toward certain acids, the nitrate and oxalate being particularly characteristic salts. In the common method for extraction of urea from urine, it is precipitated from the urine (previously concentrated by evaporation) by treatment with nitric acid. The urea is liberated from the nitrate by treating the latter with barium carbonate.

EXPERIMENT. (1) Synthesize urea as follows: Heat 25 gm. of potassium cyanide in an iron dish until it begins to fuse (do this under a hood), then add gradually 70 gm. of red oxide of lead a little at a time, stirring in well. When the frothing ceases pour on to an iron plate.

When it is cool powder the mass, separating out the metallic lead. Digest this crude cyanate for an hour with 100 c.c. of cool water. Filter through a plaited filter into an evaporating dish. Add to the filtrate 25 gm. of ammonium sulphate which has been dissolved in a small quantity of water. Evaporate to dryness on a water bath, stirring frequently to prevent crusting over. Cool the residue and powder it in a mortar. Transfer it to a small flask, add 100 c.c. of alcohol, attach to a reflux condenser, and boil for fifteen minutes. Filter off the hot alcohol into an evaporating dish. Use 25 c.c. more of alcohol in a similar manner. Evaporate the alcohol on a water bath to very small bulk. When cool, urea crystals should form. Test a few crystals or some of the solution as below.

(2) *Urea tests.* (a) Put one drop of concentrated urea solution on a glass slide; mix with it one drop of colourless concentrated nitric acid. Place a cover-glass over the crystals and examine under a microscope.

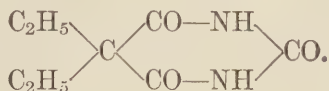
(b) In a test-tube melt some dry urea, then heat gently for a minute while gas (NH_3) is being evolved. Cool; add 1 c.c. of water, then an equal amount of 20% NaOH solution, and finally a small drop of very dilute copper sulphate solution. A violet or pinkish colour is obtained. This is called the biuret reaction (see above):



If the heating has been continued beyond a certain point an insoluble compound, *cyanuric acid*, $(\text{HCNO})_3$, is formed; this results from the combination of one

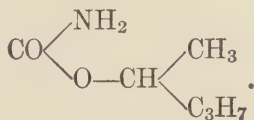
molecule of biuret with one of urea, 2NH_3 being eliminated.

Veronal is a urea derivative, being diethylmalonylurea or diethylbarbituric acid.

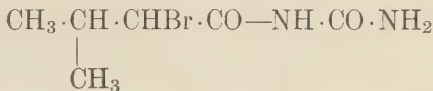


This is used as a hypnotic. The sodium salt of veronal is also used for the same purpose.

Another hypnotic related to urea is hedonal, which is really a carbamate similar to urethane. **Hedonal** is methylpropylcarbinolurethane:



Bromural is another hypnotic, derived from urea. It is monobrom-iso-valeryl-urea,

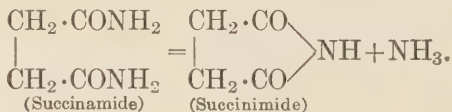


CHAPTER XIX.

MIXED COMPOUNDS (*Continued*). ACID IMIDES. COMPLEX AMIDO AND IMIDO COMPOUNDS, INCLUDING POLYPEPTIDES.

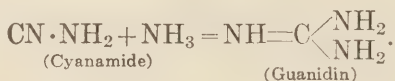
ACID IMIDES.

THESE contain the group NH; they are illustrated by succinimide, $\begin{array}{c} \text{CH}_2\text{---CO} \\ | \\ \text{CH}_2\text{---CO} \end{array} \text{NH}$. They are formed from acid amides by loss of ammonia, the amide of a dibasic acid being necessary:



OTHER AMIDO AND IMIDO COMPOUNDS.

Guanidin, $\text{NH}=\text{C} \begin{array}{l} \text{NH}_2 \\ \text{NH}_2 \end{array}$, may be considered as an imido derivative of urea, and might be called imido-carbamide. It can be synthesized from cyanamide and ammonia:

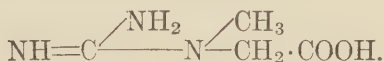


It is more strongly basic than urea, undoubtedly because of the changing of the carbonyl linking of urea for the naturally basic NH group. *Methylguanidin*.

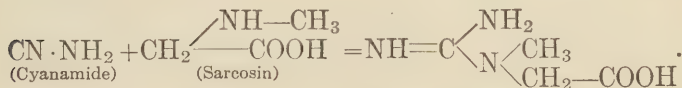


occurs as a ptomaine (p. 192). Of more importance are the derivatives of guanidin, namely, *creatin* and *creatinin*.

Creatin is methylguanidinacetic acid,

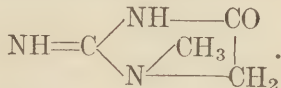


Creatin can be synthesized from cyanamide and sarcosin:



Creatin is present in considerable quantity in muscular tissue. It can be obtained from meat extract. Heating with baryta water converts it into urea, sarcosin, and some other substances. Heating with dilute acid changes it to creatinin. As a rule the appearance of creatin in the urine is pathological. It is reported as occurring normally in the urine of children.

Creatinin is creatin less a molecule of water:

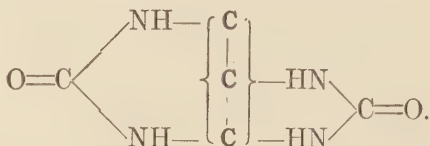


This is always present in normal human urine, about 1.5 gm. being excreted in twenty-four hours. The amount excreted when creatinin containing food (flesh) is debarred from the diet seems to be fixed a quantity

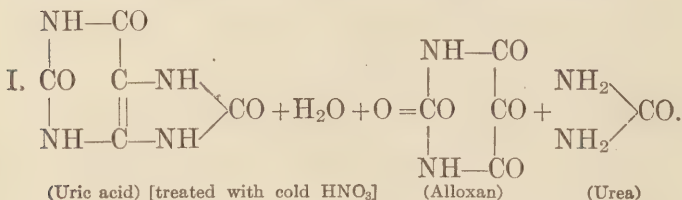
for each individual, no matter how much the total nitrogen content of the urine may vary.

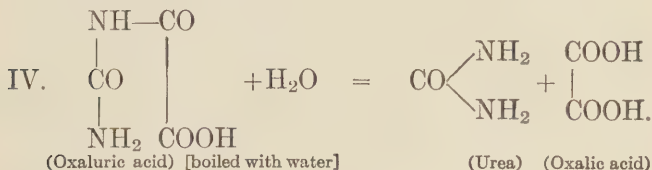
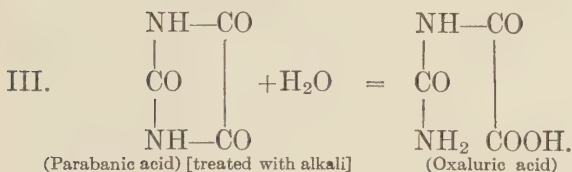
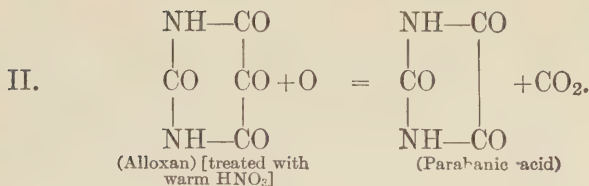
Creatinin crystallizes in monoclinic prisms. It is readily soluble. In alkaline solution it becomes converted, at least in part, into creatin. It reduces Fehling's and other alkaline copper solutions, but it holds cuprous oxide in solution; on account of these properties it may mislead in testing for sugar if the urine is concentrated. An alkaline bismuth solution, however, is not reduced by creatinin. Creatinin is precipitated by mercuric chloride and by zinc chloride, these reagents entering into chemical union with the creatinin.

Uric acid is a derivative of urea. In uric acid two molecules of urea unite together by linking to an intermediate carbon chain, each NH_2 group losing one hydrogen atom and becoming NH in order to effect the union:



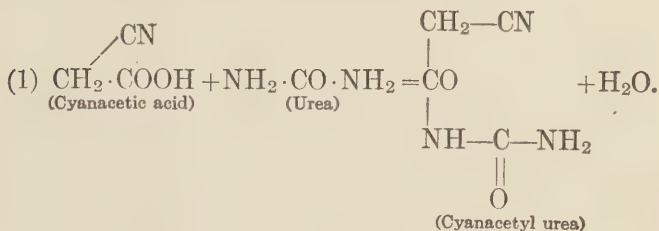
This is the skeleton of the uric acid formula. The presence of two urea molecules and of a carbon chain is shown by the nature of the decomposition products of uric acid resulting from oxidation and hydrolysis:



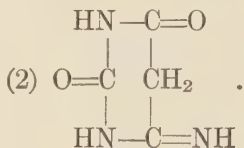


The presence of the pyrimidin ring, $\begin{array}{c} \text{N}-\text{C} \\ | \quad | \\ \text{C} \quad \text{C} \\ | \quad | \\ \text{N}-\text{C} \end{array}$, in uric

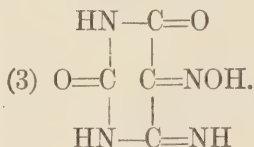
acid is shown by *Traube's synthesis*, which is as follows: Cyanacetic acid and urea are treated with POCl_3 ; the latter removes hydroxyl from the acid, and urea takes its place to form cyanacetyl urea:



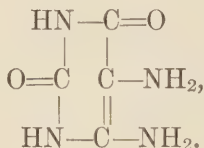
Treating cyanacetyl urea with alkali causes a shifting within the molecule, resulting in the formation of the pyrimidin derivative,



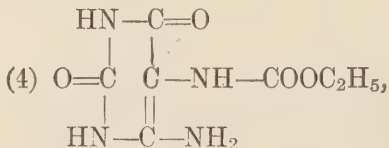
This is treated with HNO_2 , giving



By reduction this becomes

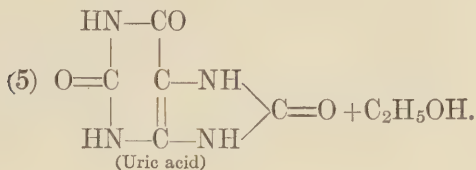


which when acted on by $\text{CClOOC}_2\text{H}_5 + \text{KOH}$ gives
(Ethyl chlorcarbonate)



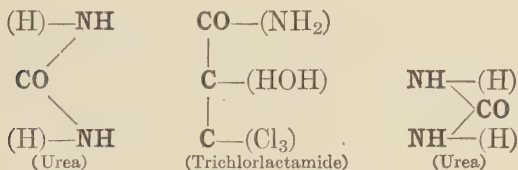
a pyrimidin derivative of urethane. The potassium salt of this is heated (dry) to 150° , then later to 180° —

190°. Alcohol is split off, leaving uric acid (as potassium urate):



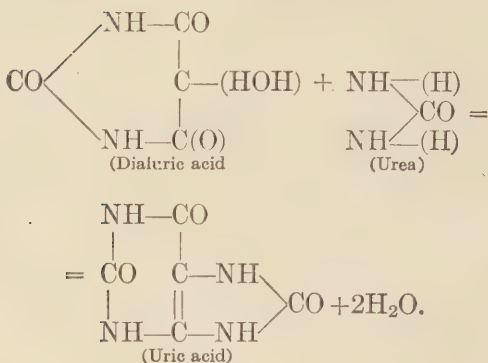
This synthesis conclusively proves the structure of uric acid.

Another interesting synthesis, because it is analogous to one which may occur in the animal body, (at least in birds), is effected by heating together urea and trichlorolactamide:



The groups in parenthesis do not enter into the uric acid molecule, but unite to form NH_4Cl , HCl , and H_2O .

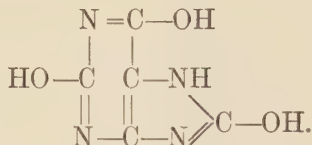
Dialuric acid, $\text{CO} \begin{array}{c} \text{NH}-\text{CO} \\ \diagdown \quad / \\ \text{NH}-\text{CO} \end{array} \text{CHOH}$, appears in the case of birds to be an intermediate body in the synthesis of uric acid by the liver. It is formed by the combination of urea with tartronic acid (p. 205). By the addition of another urea molecule to this, uric acid is produced:



Analogous synthesis in the case of mammals has not been proven.

Uric acid has been synthesized by heating together glycocoll and urea. On the other hand, uric acid when heated in a sealed tube with HCl yields glycocoll.

Tautomerism of uric acid. Uric acid exists not only in the form corresponding to the above formula (the *lactam* state) but also in another form (the *lactim* state) in which the three O atoms are in hydroxyls:



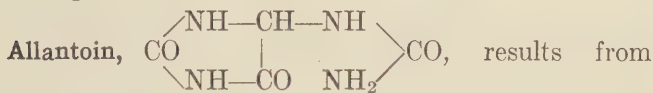
The lactam form is less stable. It is stated that in the urine uric acid is in the lactim form.

Uric acid acts as a weak dibasic acid, forming urates. It does not, however, play any part in the acid reaction of urine. It is believed to exist mainly in the form of monosodium urate in both the blood and the urine.

It often crystallizes out as a reddish deposit from strongly acid urine. About 0.7 gm. is excreted daily by man. Pure uric acid is a colourless crystalline powder. It is almost insoluble in cold water and alcohol. Uric acid reduces Fehling's solution, but does not reduce an alkaline bismuth solution.

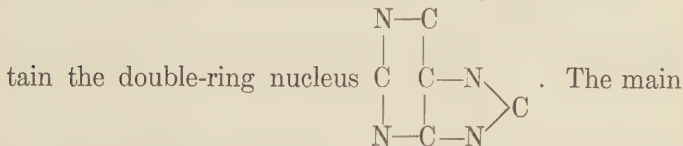
EXPERIMENT. (1) Add 5 c.c. of 20% HNO_3 to a little uric acid in an evaporating-dish; evaporate to dryness on a water bath. Alloxantin is formed. To the residue add baryta water; a blue colour appears.

(2) Repeat the above, but instead of using baryta expose the residue to fumes of ammonia. A red colour is obtained, due to murexide. This test is called the murexide test. If much ammonia is present in the air, the residue will be reddish because of the ammonia taken up.



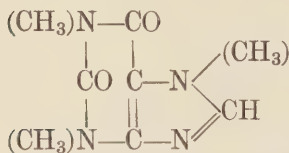
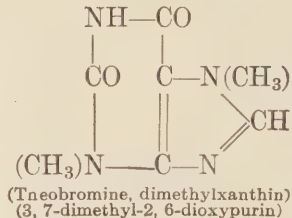
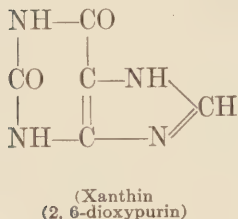
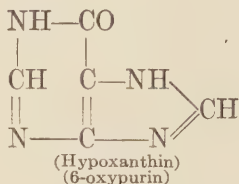
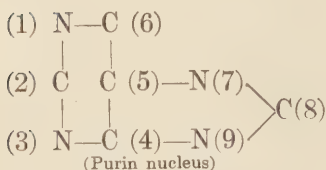
careful oxidation of uric acid by potassium permanganate. It occurs in the urine of calves, and at times in human and in dogs' urine.

Purin bodies. Uric acid and all the *purin bodies* con-

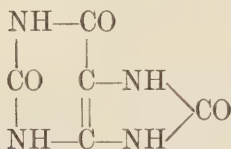


ring is the pyrimidin ring; the purin nucleus, therefore, is pyrimidin with a urea residue attached as a secondary ring. The relationship of the purin bodies is shown below:

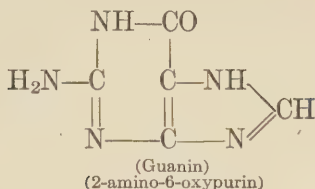
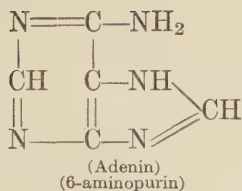
Purin itself has an H atom at each of the positions numbered 2, 6, 7, and 8. It can be prepared from uric acid.



(Caffeine, theine, trimethylxanthin) (1, 3, 7-trimethyl-2, 6-dioxypurin)



(Uric acid) (2, 6, 8-trioxypurin)



There are a number of methyl purins besides caffeine and theobromine, as, 1 methyl xanthin, 7 methyl xanthin (heteroxanthin), 1, 7 dimethyl xanthin (paraxanthin), and 7 methyl guanin.

The purins are also called *alloxuric*, *xanthin*, or *nuclein* bodies.

Caffeine and theobromine when taken as food are excreted in the urine partly unchanged and partly as monomethyl and dimethyl xanthins. Only 35–40 per cent of caffeine and theobromine appear in the urine as purin bodies. A number of investigators agree in the assertion that tea and coffee do not increase uric acid excretion. The other purins are excreted mainly as uric acid. It is believed by some that on a diet which is free of purin bodies the amount of purins excreted daily is a fixed quantity for each individual (*cf.* creatinin).

Some of the purins, mainly xanthin and hypoxanthin, are found in muscle, and therefore in meat extract. *Beef tea* or a solution of *meat extract* contains as its organic constituents chiefly creatin, purin bodies, and sarcolactic acid.

Theobromine (dimethylxanthin) is found in chocolate and cocoa. It is called an alkaloid (see p. 382).

Caffeine or **theine** (trimethylxanthin) is the alkaloidal

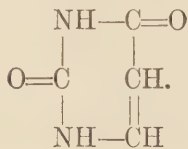
principle in tea and coffee. Both theobromine and caffeine are used as medicines.

EXPERIMENT. Try the murexide test (see p. 235) on a little caffeine. Repeat, substituting bromine water for HNO_3 .

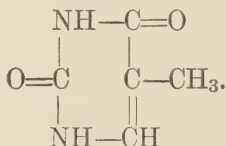
Pyrimidin derivatives. These are derived from nucleic acid by hydrolysis whether by the action of acids or by post-mortem autolysis of animal tissue.

The most important are uracil, thymin and cytosin.

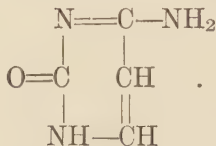
Uracil is 2, 6 dioxypyrimidin,



Thymin is 5, methyl 2, 6 dioxypyrimidin,



Cytosin is 6 amino 2 oxypyrimidin,



As an illustration of a **nucleic acid** might be mentioned one which has been obtained from a nucleoprotein of the thymus gland. It is believed to consist of the

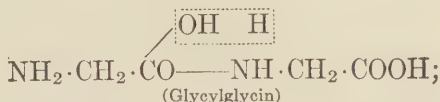
linking together of four hexose (p. 246) and four metaphosphoric acid molecules with one molecule each of guanin, adenin, thymin and cytosin. To it has been assigned the formula:



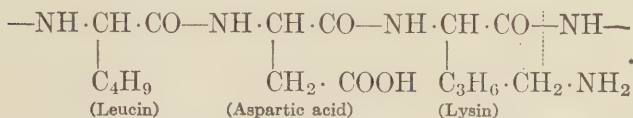
Leucomaine is a term applied to basic substances found in living animal tissues. The purin bodies and the creatinin group of compounds are the chief leucomaines.

DIPEPTIDES AND POLYPEPTIDES.

Because of the fact that the decomposition products of proteins include amino-acids (as alanin, glycocoll, leucin, tyrosin, aspartic acid, etc.) and the hexone bases, it has been proposed to explain the structure of the protein molecule as a chaining together of these amino bodies by means of the removal of OH of a carboxyl group of the one amido body and an H of the amido group of another (*cf.* formation of acid amides), thus:



or a more complicated chain, as:



Of course the above is supposed to be only a part of the formula.

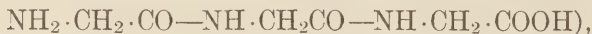
This theory of the constitution of protein molecules gives the best explanation of the universality of the biuret test as applied to proteins (see p. 226), the test being due to the many $\text{—NH}\cdot\text{CH}\cdot\text{CONH—}$ groups (cf. glycynamide, p. 221).

On the basis of this hypothesis the problem of the synthesis of protein is now being vigorously attacked. Compounds have been synthesized in which two, three, and even up to eighteen molecules have been made to combine in this manner; these synthetic bodies are called peptides.

If two molecules have united, the compound is a dipeptide; for example, glycylglycin,



Polypeptides are built up from more than two molecules; they include tripeptides (as diglycylglycin,



tetrapeptides, pentapeptides, hexapeptides, etc.

A polypeptide composed of three leucin and fifteen glycocoll molecules has been synthesized, the formula being $\text{C}_{48}\text{H}_{80}\text{O}_{19}\text{N}_{18}$ and the molecular weight 1213.

Certain polypeptides, identical with those produced synthetically, have been obtained by partial hydrolysis of proteins. The more complex polypeptides show certain resemblances to peptones in their reactions. They taste bitter. They are precipitated by the same reagents, and give the biuret test. Those that are composed of amino acids of the same optical activity as those occurring in proteins, are hydrolyzed by trypsin.

E. Fischer, who is doing such brilliant work in this line of synthesis, is inclined to doubt whether this comparatively simple method of linking is the only kind of linking existing in protein molecules.

PROTEINS.

Proteins are complex nitrogenous compounds that yield on complete hydrolysis mainly amino acids, hexone bases (p. 216) and ammonia. They vary widely in the proportion of the different amino acids and bases, contained in their molecules, e.g., hæmoglobin has not less than 20 per cent of leucin, but gelatin only about 2 per cent; on the other hand there is 16.5 per cent of glycocoll in gelatin and none in hæmoglobin.

The most important classes of proteins are protamines, histones, albumins, globulins, phosphoproteins, scleroproteins, compound proteins (chromoproteins, glucoproteins and nucleoproteins), derived proteins (coagulated proteins, acid and alkali metaproteins, proteoses and peptones) and certain classes of vegetable proteins called glutelins and prolamines (or gliadins).

Iodothyrim (thyreiodin) is a derivative of an iodine containing protein, present in thyroid tissue.

Oxyproteic acid, $C_{43}H_{82}N_{14}O_{31}S$, is a derivative of protein. It is found in the urine, and may be greatly increased in some pathological conditions.

CHAPTER XX.

MIXED COMPOUNDS (*Continued*). CARBOHYDRATES AND GLUCOSIDES.

CARBOHYDRATES.

THIS last class of mixed compounds is of very great importance, since it includes sugars and starches. The name *carbo(n)hydrates* calls attention to the fact that the number of atoms of hydrogen and oxygen present in the molecule bear the same ratio to one another as in water;¹ therefore a general formula often given for carbohydrates is $C_n(H_2O)_m$.

This, however, is misleading, for there are a number of non-carbohydrate substances that conform to this formula, such as acetic acid, $C_2H_4O_2$, and lactic acid, $C_3H_6O_3$.

Carbohydrates may be defined as including monosaccharides and those more complex substances that yield by hydrolysis simply monosaccharides.

All monosaccharides contain in their formulæ a CO group, either in an aldehyde group or as the ketone group, and have also an alcoholic hydroxyl attached to each of the other carbon atoms.

There are four classes of carbohydrates, namely, *monosaccharides*, *disaccharides*, *trisaccharides* and *polysaccharides*.² Monosaccharides are the simplest car-

¹ It should be pointed out in this connection that the term hydrate as applied to alkalies is inaccurate, e.g., NaOH, sodium hydroxide, not a hydrate.

² These are also called monoses, bioses, trioses and polyoses.

bohydrates. From the linking together of two monosaccharide molecules disaccharides result. A trisaccharide contains in its molecule three monosaccharide molecules. Polysaccharides have complex molecules that can be resolved into many monosaccharide molecules.

MONOSACCHARIDES.

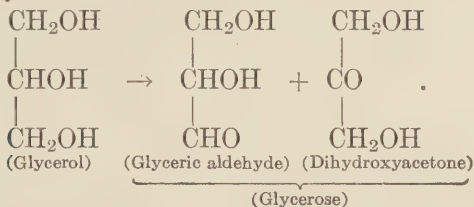
According to the number of carbon atoms present, monosaccharides are called dioses, trioses, tetroses, pentoses, hexoses, heptoses, octoses, and nonoses.

Aldoses are those containing an aldehyde group, while *ketoses* are those having a ketone group.

$$\begin{array}{c} \text{CH}_2\text{OH} \\ | \\ \text{Glycol aldehyde, } \left| \begin{array}{c} \text{CHO} \end{array} \right. \end{array}$$

, may be considered a **diose**.

Glycerose can be obtained by mild oxidation of glycerol (or lead glycerate); it is a mixture of an aldehyde and a ketone, and since each contains three carbon atoms, they are **trioses**:

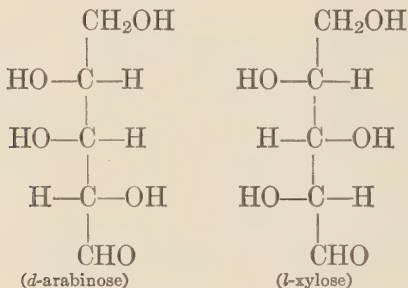


$$\begin{array}{c} \text{CH}_2\text{OH} \\ | \\ \text{CHOH} \\ | \\ \text{CHOH} \\ | \\ \text{CHO} \end{array}$$

Tetrose, $\left| \begin{array}{c} \text{CHOH} \end{array} \right|$, can be obtained by polymerization

of glycol aldehyde. A ketose tetrose also occurs.

The chief **pentoses** are *d*-arabinose and *l*-xylose. The following formulæ represent their isomeric relation:



Arabinose is obtainable by boiling gum-arabic with dilute acid. **Xylose** can be obtained by similar means from bran or wood. Racemic arabinose is sometimes present in the urine as an abnormal constituent. Several ketose pentoses are known.

On account of having three asymmetric C atoms four main arrangements and the mirror images of these are possible, so that eight aldose pentoses are obtainable. Seven of these are known at present.

Both arabinose and xylose reduce Fehling's solution and form osazones with phenylhydrazine (the nature of the osazone reaction will be explained presently). Neither is fermented by pure yeast. They give certain colour reactions which will be illustrated in the experiment below.

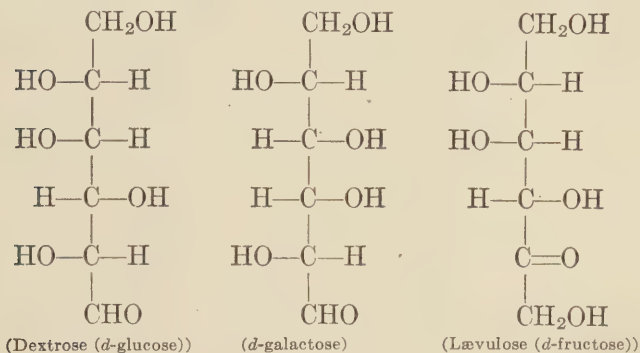
Most of the monosaccharides thus far considered have not been found in natural products.

Several methyl derivatives of monosaccharides occur in glucosides, as *digitoxose*, $\text{C}_6\text{H}_{12}\text{O}_4$, a dimethyltetrose,

digitalose, $C_7H_{14}O_5$, a dimethylpentose, and *rhamnose*, $C_6H_{12}O_5$, a methyl pentose.

EXPERIMENT. *Pentose test.* To 2 c.c. of water in a test-tube add 2 c.c. of HCl and warm. Add phloroglucin, a little at a time, as long as it dissolves. Now add 1 c.c. of arabinose solution, and heat until a red colour is obtained; examine at once with a small spectroscope, when an absorption band between the *d* and *e* lines will be seen. Heat until a precipitate forms, add some amyl alcohol, and shake—the alcohol becomes coloured and gives the same spectroscopic appearance as above.

The **hexoses** are the sugars of prime importance. The chief ones are *dextrose*, *galactose*, and *lævulose*; the first two are *aldoses*, while the last is a *ketose*:

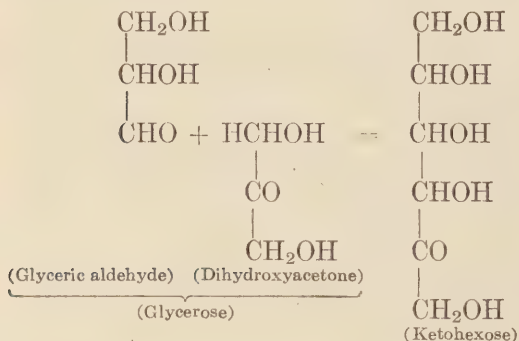


The aldoses have four asymmetric C atoms, therefore eight main arrangements of the secondary alcohol groups together with their mirror images make sixteen aldose hexoses possible. Twelve of these have been studied.

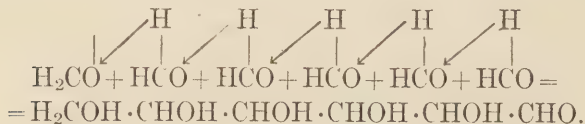
d-Mannose differs from *d*-glucose only in the arrangement of the fourth secondary alcohol group. The mirror image aldoses are the *l*-hexoses and are lævorotatory. Lævulose is called *d*-fructose because the arrangement of its secondary alcohol groups is the same as in *d*-glucose.

Six ketose hexoses are known, the only one of importance being lævulose. Two methyl hexoses have been prepared.

Condensation of the aldehyde and ketone trioses in glycerose results in the production of a ketose isomeric with lævulose, thus:



Such condensations are commonly called aldol condensations (see aldol, p. 127). By aldol condensation of six molecules of formaldehyde, formose is obtained, which contains an aldose identical with that obtained from glyceric aldehyde:



All the synthetic sugars are optically inactive when produced by purely chemical means.

Physiologists believe that in the animal body glycerol (from fat) may be converted into a hexose, at least under certain circumstances.

Dextrose is the aldehyde of the hexacid alcohol *sorbitol*, $\begin{array}{c} \text{CH}_2\text{OH} \\ | \\ (\text{CHOH})_4 \\ | \\ \text{CH}_2\text{OH} \end{array}$, and can be converted into the latter by

reduction. Dextrose can be oxidized to the dibasic

acid *saccharic acid*, $\begin{array}{c} \text{COOH} \\ | \\ (\text{CHOH})_4 \\ | \\ \text{COOH} \end{array}$. The alcohol *dulcitol*, a

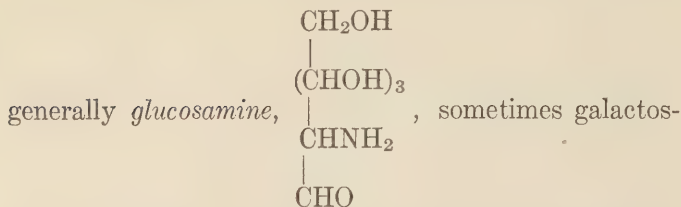
stereoisomer of sorbitol, can be oxidized to galactose, and this aldehyde monosaccharide can be oxidized fur-

ther to *mucic acid*, $\begin{array}{c} \text{COOH} \\ | \\ (\text{CHOH})_4 \\ | \\ \text{COOH} \end{array}$. Similarly there are

alcohols and acids corresponding to the other hexoses.

Glycuronic acid (p. 204) is a monobasic acid, having the same arrangement of the CHOH groups as *d*-glucose, the aldehyde group also being present.

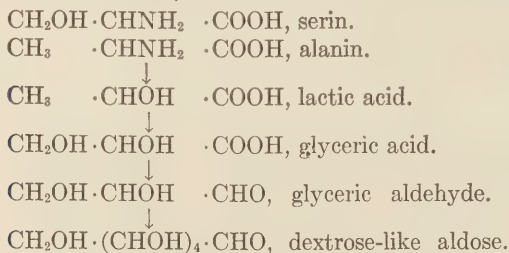
There are certain proteins that contain a carbohydrate derivative combined with the protein molecule proper: such are called **glucoproteins**. This combined sugar has been found in most cases to be an aminohexose,



amine. *l*-Xylose is found in combination in nucleoproteins. The sugar group in protein may be detected by certain colour reactions (see exp. below).

The question of the possibility of the formation of dextrose from proteins other than glucoproteins is of very great physiological importance. The chemistry of the problem will now be briefly considered. Attention has been called to the fact that proteins readily split up into amino-acids. Reasoning on purely chemical grounds it is possible that amino-acids containing three or six carbon atoms can be converted into dextrose.

Alanin can be changed to lactic acid, the latter to glyceric acid, which can be reduced to glyceric aldehyde, and finally this can be converted into a dextrose-like sugar by aldol condensation. Such a synthesis when carried out in the animal organism would undoubtedly result in production of dextrose, i.e., dextrorotatory glucose. It is quite likely that serin is also convertible into lactic acid and therefore into dextrose:



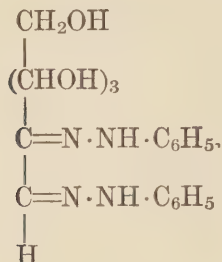
The production of dextrose from alanin, glycocoll, aspartic acid and glutaminic acid in the animal body has been experimentally demonstrated, lactic acid being noted as an intermediate product.

EXPERIMENT. To 1 c.c. of a strong solution of egg proteid add a drop of saturated solution of α -naphthol in alcohol (acetone-free); then with a pipette add 1 c.c. of C.P. H_2SO_4 , so that the acid does not mix, but forms a bottom layer. The greenish colour at the zone of contact is due to the reagents; let the tube stand until a violet ring forms. If the violet colour does not appear, tap the tube so as to cause a slight mixing of the two layers. This is *Molisch's test* and is given by all carbohydrate-containing substances.

Instead of the alcoholic solution a 10% solution of α -naphthol in chloroform may be used.

General Reactions of Monosaccharides. They all reduce alkaline silver, copper, and bismuth solutions, as do other aldehydes and some ketones (see p. 129). All form osazone crystals when treated with phenylhydrazine acetate (see exp. below). The reaction occurs in two stages, first the O of CO is substituted (as in hydrazones), then secondly the excess of phenylhydrazine removes two H atoms of the neighboring CHOH group, converting it to CO and the latter reacts with phenylhydrazine. The osazone from lævulose is identical chemically with that from dextrose, because lævulose has the same arrangement of CHOH groups as dextrose, and the end CH_2OH is changed to CO in this case. In similar manner *d*-mannose gives an osazone which is the same as glucosazone.

Methylphenylhydrazine gives osazones only with ketoses, and can therefore be used to detect the presence of lævulose. Glucosazone has the formula



This can be converted by treatment with warm hydro-

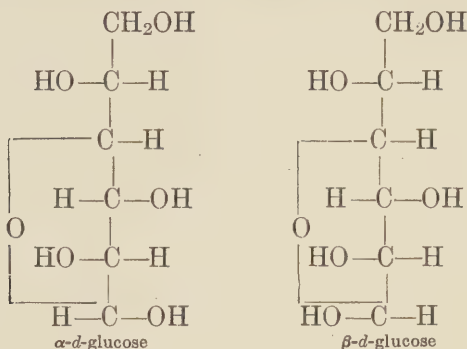
chloric acid into glucosone,
$$\begin{array}{c}
 \text{CH}_2\text{OH} \\
 | \\
 (\text{CHOH})_3 \\
 | \\
 \text{CO} \\
 | \\
 \text{CHO}
 \end{array}$$
 When glucosone

is treated with nascent hydrogen (as by using zinc dust), fructose is formed. Thus we can convert an aldose into a ketose.

Dextrose and galactose are dextrorotatory; lævulose is lævorotatory. They all have a different rotary power when freshly dissolved from that which they show after allowing the solution to stand. This phenomenon is called *mutarotation* or *multirotation*.

This has been explained by supposing a lactone-like linking in the sugar molecule so that the C of the aldehyde group comes to hold H and OH. This C atom is now asymmetric and two stereoisomers become possible, designated as α and β . This has been investigated

in the case of *l*-arabinose, *d*-galactose, lactose and *d*-glucose. This will be illustrated by *d*-glucose:



The α variety, immediately after preparing a solution, has a specific rotation (p. 260) of 110° , the β variety 19° , on standing each solution changes and both finally come to a specific rotation of 52.7° ; α partly changes to β and α partly changes to α , the two come into equilibrium when 40% of the glucose is α and 60% β . Maltose is believed to be made up of two α -*d*-glucose molecules and isomaltose of two β -*d*-glucose molecules. The apparent conversion of the aldehyde group into a secondary alcohol group does not prevent the compound giving aldehyde tests.

These hexoses are fermented by yeast, giving, as the main products, alcohol and carbon dioxide. *l*-Glucose does not ferment, possibly because the optically active enzyme *fits* only the *d*-form.

In making a test for reducing sugar (dextrose, lævulose, pentose or lactose) in the urine, reduction of Fehling's solution is not sufficient, for the urine may reduce this reagent slightly after the administration of turpentine, chloroform, chloral,

phenacetin, saccharin, salicylic acid and balsams, because these bodies are excreted in glycuronic acid combination (see p. 204). While the bismuth test excludes many non-saccharine substances (uric acid and creatinin) that reduce Fehling's solution, it may yet be positive with urine after the administration of antipyrin, salol, turpentine, kairin, senna, rhubarb, benzosol, sulphonal, trional and some other drugs. The phenylhydrazine test is the most delicate and the most positive. The fermentation test, if positive, is conclusive evidence. If lactose or a pentose alone be present, fermentation will not occur. These can be distinguished by a special pentose test, and in the case of lactose by increase in dextrotation after boiling with dilute HCl (hydrolysis).

Lævulose can be differentiated from dextrose by the special ketose test and by lævorotation. Chloroform added to urine as a preservative gives reduction because heating it with alkali produces formic acid.

Normal urine has a reducing power equivalent to 0.2% dextrose, but less than one-fifth of this is due to dextrose.

Dextrose (glucose, grape sugar) is present in many fruits and plants, in honey, and in the urine of diabetic patients. Commercial glucose is made by boiling starch with dilute acid; it is used for making candies, cheap syrup, etc. Pure glucose is crystalline; if crystallized from water it contains a molecule of water of crystallization, but if crystallized from methyl alcohol it is anhydrous. It is not so sweet as cane sugar.

Galactose is obtained from lactose, by hydrolysis of the latter. It ferments slowly.

Lævulose (fructose, fruit sugar) is contained in many sweet fruits, in honey, and rarely in urine. It is difficult to crystallize. Its rotary power is greatly dependent on temperature and concentration.

EXPERIMENTS. (1) Prepare *osazone* crystals from dextrose and lævulose as follows: To 100 c.c. of a strong solution of the sugar add 0.25 gm. of phenylhydrazine hydrochloride and 0.5 gm. of sodium acetate, heat in a boiling water bath for an hour, and cool. Examine the yellow crystals under the microscope. Collect the crystals on a filter, wash thoroughly with water acidulated with acetic acid, or with cold acetone, press between filter-paper, recrystallize from a little 80% alcohol, dry the crystals in a desiccator, and later make melting-point determinations.¹

The osazones of the important sugars have the following melting-points:

Dextrose	}	 204°-205°
Lævulose		
Lactose.....		200°
Maltose.....		206°

(2) *Ketose test.* To a few cubic centimetres of lævulose solution add half its volume of HCl. Add a few crystals of resorcin and heat the mixture. A deep-red colour develops, later a brown precipitate which is soluble in alcohol. The alcoholic solution is red.

(3) (a) Try the aldehyde tests (see p. 106) with dextrose solution. (b) To some dextrose solution add one fifth its volume of alkaline bismuth reagent (4 gm. Rochelle salts and 2 gm. of bismuth subnitrate dis-

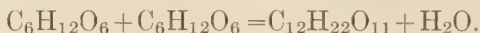
¹ A quicker and more satisfactory way of securing osazone crystals is as follows: To 0.5 c.c. phenylhydrazine add 0.5 c.c. glacial acetic acid, after mixing add 10 c.c. of the sugar solution, heat in a boiling water bath; glucosazone crystals appear in 5-10 minutes. For lact- and maltosazone heat 20-30 minutes, then cool before examining.

solved in 100 c.c. of 10% NaOH), boil five minutes. On cooling a black precipitate separates out.

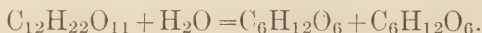
Several *heptoses* and *octoses* and two *nonoses* are known, but they are unimportant.

DISACCHARIDES.

These are the result theoretically of the union of two monosaccharide molecules, with the elimination of a molecule of water, cane sugar being a combination of dextrose and lævulose, lactose of dextrose and galactose, and maltose of two α -*D*-glucose molecules:



By hydrolysis the constituent monosaccharides are easily obtained:



Dilute mineral acids and ferments (invertases) bring about this hydrolysis, which is called *inversion*. Yeast produces an invertase that hydrolyzes maltose quickly and another which hydrolyzes cane sugar slowly, but none that has an effect on lactose. Therefore lactose does not ferment with yeast, while cane sugar and maltose do.

Inversion by the action of dilute mineral acids is due to catalytic action of hydrogen ions, just as in the case of hydrolysis of esters (p. 156) (see appendix, p. 410).

Maltose and lactose reduce alkaline copper and bismuth solutions; pure cane sugar does not. After inversion, however, cane sugar reduces these reagents. Therefore Fehling's solution can be used for quantitative

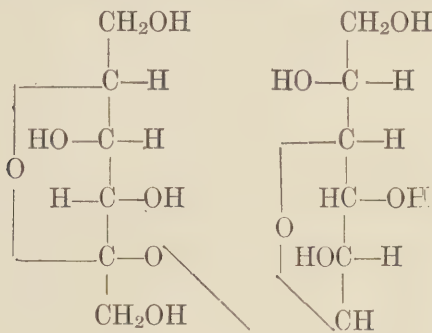
estimation of all the sugars treated of in this chapter. 10 c.c. of Fehling's solution is reduced by

0.050	gram dextrose or lævulose.
0.0676	“ lactose.
0.074	“ maltose.
0.0475	“ cane sugar (after conversion into invert-sugar).

A solution of copper acetate acidified with acetic acid (Barfoed's reagent) is not reduced to cuprous oxide by disaccharides, but gives reduction with monosaccharides.

Maltose and lactose form osazones with phenylhydrazine, each of these having a characteristic crystalline form and melting-point (see p. 254), while cane sugar forms no such combination provided hydrolysis is guarded against.

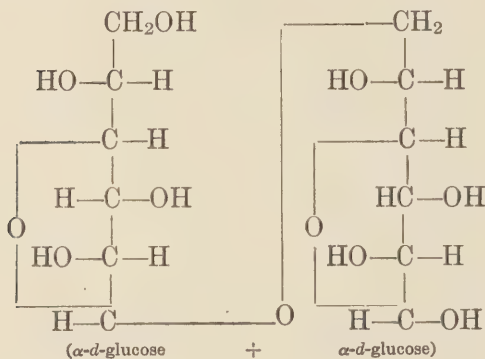
In order to explain the non-aldehydic action of cane sugar as shown by its behaviour in these two reactions the following formula has been suggested for it:



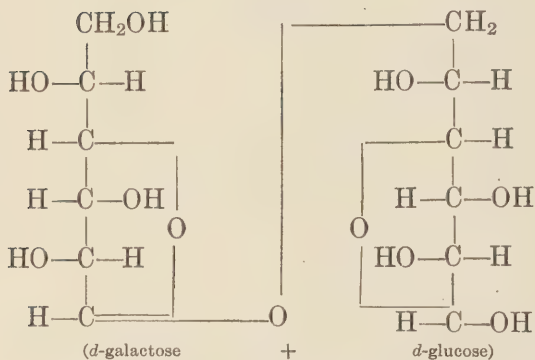
Both the aldehyde and ketone groups are tied up by the linking together of their C atoms.

The other disaccharides have the following formulæ:

Maltose.



Lactose.



These disaccharides are all dextrorotatory. Maltose shows the greatest rotary power, lactose the least; maltose and lactose manifest multirotation. Invert-sugar is distinctly lævorotatory, while the cane sugar from which it is produced is dextrorotatory; this is due to the fact that the lævulose produced (invert-

sugar is a mixture of equal parts of lævulose and dextrose) rotates polarized light more to the left than does dextrose to the right.

The rotary power of maltose is decreased by inversion, while that of lactose is increased.

Saccharose (cane sugar, beet sugar, sucrose), $C_{12}H_{22}O_{11}$, is the most important of the sugars because of its use as food. It is contained in sugar cane, beets, the sap of certain maple trees, and in many other vegetables and plants.

The method of commercial preparation of cane sugar is, in brief, as follows: The crushed or chipped material is soaked with water so that the sugar diffuses out; beet chips are first heated to 80–90°, this coagulates the protein of the cell walls and causes rupture of the cells. The sugar extract is treated with lime (removes acids and many impurities), then with carbon dioxide (removes the excess of lime), and is then evaporated in vacuum pans. On cooling, sugar crystallizes out. This crude sugar is dissolved, filtered through bone-black (animal charcoal), and recrystallized. The syrup that is left is *molasses*. Cane sugar as sold is commonly called granulated sugar.

Cane sugar forms large crystals when slowly crystallized; they are monoclinic prisms. It melts at 160°; at 210°–220° it is converted into caramel with loss of water. It is extremely soluble, 100 gm. of water at 15° dissolves 197 gm. of sugar; this saturated solution has a specific gravity of 1.329. It forms saccharates with bases.

Its rotary power is influenced somewhat by concentration; it is lessened by presence of acids, alkalies or salts, but is practically uninfluenced by temperature.

Lactose (milk sugar), $C_{12}H_{22}O_{11} + H_2O$, is the sugar contained in milk. It occasionally occurs in the urine of pregnant and nursing women. Certain microorganisms convert lactose into lactic acid (souring of milk, see p. 201). When heated it forms lactocaramel, $C_6H_{10}O_5$. Lactose is crystalline and contains a molecule of water of crystallization. It can be obtained as amorphous lactose, which is anhydrous. Lactose forms compounds with bases. Its specific rotation is not influenced much by concentration or temperature.

Maltose, $C_{12}H_{22}O_{11} + H_2O$, is the product of the action of the ferments diastase (in malt), ptyalin (in saliva), or amylopsin (in pancreatic juice) upon starch. It can also be obtained from starch by treatment with dilute mineral acids, the action of the acid being stopped at a stage before glucose is formed. It crystallizes in fine needles. Its specific rotation varies with concentration and temperature.

Isomaltose (gallisin) is distinguished from maltose in that it does not ferment with yeast, and that its osazone has a lower melting-point (150°).

EXPERIMENTS. (1) Produce osazone crystals from lactose and from maltose (see p. 254). Examine microscopically. Make melting-point determinations.

(2) (a) Examine a 10% solution (10 gm. dissolved in enough water to make 100 c.c. of solution) of pure cane sugar with the polariscope (see p. 209). (b) To 50 c.c. of a 20% cane sugar solution in a 100 c.c. graduated flask add 1 gm. of citric acid, and heat in a boiling water bath for 30 minutes. Cool, almost neutralize, and fill up to the mark. Examine this invert-sugar

solution (corresponding in concentration to the solution in (a)) with the polariscope. The specific rotation $[\alpha]_D$ of the important sugars in 10% solution (at 20°) when sodium light is used are for

Dextrose (anhydrous).....	+ 52.7°
Lævulose.....	- 93.0°
Maltose (anhydrous).....	+ 137.04°
Lactose (+ H ₂ O)	+ 52.5°
Cane sugar	+ 66.54°
Invert sugar	- 20.2°

(- means rotation to the left.)

(3) Test cane sugar before and after inversion (solutions of experiment 2, *a* and *b*) with Fehling's solution.

(4) Try the ketose test (see p. 254) on cane sugar solution.

(5) *Galactose test.* To 10 c.c. of a strong solution of lactose add 3 c.c. of HNO₃ and boil for a few minutes. Now evaporate on a water bath to about 3 c.c. while stirring. Add 2 c.c. of water and cool. If no crystals of mucic acid separate out, let the material stand and examine after twenty-four hours.

The trisaccharide, raffinose, consists of *d*-fructose, *d*-glucose and *d*-galactose linked together as in saccharose, none of the CO groups being free. It therefore does not reduce Fehling's solution. Emulsin hydrolyzes it to cane sugar and galactose. Invertase of yeast hydrolyzes it, therefore it ferments. It gives the ketose test. Its specific rotation is +104°.

POLYSACCHARIDES.

These have complex molecules containing many sugar molecules linked together.

Cellulose, $(C_6H_{10}O_5)_x$, having a very high molecular weight, is essential to all plants, being the chemical basis of the woody fibre. Cotton-fibre, hemp, flax, and the best filter-paper are almost entirely cellulose. Ordinary paper is composed mainly of cellulose. Cellulose is affected by only a few chemical agents; concentrated acids and alkalies and an ammoniacal solution of copper oxide (Schweitzer's reagent) are able to dissolve it. If unsized paper be treated momentarily with sulphuric acid, its surfaces become changed to *amyloid*, which renders the paper tough. Parchment paper is made in this way. If a solution of cellulose in sulphuric acid be diluted and boiled, dextrin and glucose are produced by hydrolysis of the cellulose.

EXPERIMENTS. (1) Dissolve some scraps of filter-paper in a little cold concentrated H_2SO_4 , dilute with 200 c.c. of water, and boil for an hour. Neutralize some of this hydrolyzed cellulose solution and test with Fehling's solution.

(2) Immerse a piece of blotting-paper in 80% H_2SO_4 for a moment only, transfer to a large beaker of water, and wash out the acid thoroughly. Allow the paper to dry out; it will be found to be tough.

(3) Detection of lignin ¹ in paper made from wood.

¹ A substance (probably not a polysaccharide) present along with cellulose in wood.

Coat a sheet of cheap white paper with a solution of aniline in HCl; if it turns yellow, lignin is present.

When cellulose is treated with nitric acid in the presence of sulphuric acid, **nitro-celluloses** are formed, just as nitroglycerol is produced from glycerol. These range from mononitro to trinitrocellulose.

Guncotton (nitrocellulose, pyroxylin) is trinitro-cellulose. It is explosive. By dissolving guncotton in acetone a gelatinous mass is obtained, then on removing the solvent, the guncotton is left in such a physical condition that it burns and explodes more slowly. This substance is used in smokeless powders. The products of the explosion are nitrogen, hydrogen, carbon monoxide and dioxide, and water-vapour.

The two lower nitrates are contained in *celloidin*. *Colloidion* is a solution of these nitrates in a mixture of ether and alcohol. *Celluloid* is made by dissolving them in camphor.

An artificial silk can be produced by means of trinitrocellulose, fine filaments being made and spun into thread. After being woven the nitrocellulose fabric is treated with a solution of calcium sulphide, which removes the NO_2 groups. Almost pure cellulose, resembling silk, is left.

EXPERIMENT. Mix 5 c.c. of C.P. HNO_3 and 10 c.c. of C.P. H_2SO_4 . When cool immerse some absorbent cotton in the mixture for half a minute, then wash out the acid from the cotton with a large quantity of water, press out the water, and dry at room temperature. When dry, shake part of it with a mixture of ether and alcohol, pour the liquid into an evaporating dish and allow to evaporate. A syrupy liquid (collodion) is

obtained, and later a glassy skin. Test the inflammability of another piece of the dry cotton, and compare with untreated cotton.

Starch (*amylum*), $(C_6H_{10}O_5)_x$, comprises a large part of all vegetable food. It exists in the plant as granules, having different forms and sizes in different plants. Starch grains are supposed to consist of more or less spherical masses of radiating interwoven acicular crystals. When heated with water, the latter is absorbed by the crystals so that the granules swell.

Starch and cellulose are probably synthesized by plants from formaldehyde by processes of condensation and polymerization.

Ordinary starch is made from corn or potatoes. Starch is insoluble in cold water. When boiled, it apparently goes into solution or forms a gelatinous mass, according to the amount of water present. It is not a true solution, however, but is called a colloidal solution.

It is precipitated from solution by low concentration of alcohol, and by saturation with certain salts (as Na_2SO_4 and $NaCl$). A dilute solution of boiled starch is readily hydrolyzed by ferments (diastase, ptyalin, etc.) and by platinum black (catalytic action) at a temperature of about 40° . Dextrin is first formed, then maltose, while hydrolysis by boiling with dilute mineral acid carries the process further, the end product being glucose. Heat alone converts starch into dextrin; the crust on bread is mainly dextrin. Starch combines with iodine to form a blue compound; heat drives the iodine out of combination, so that the colour is lost until the mixture becomes cool again. Natural starch contains two different compounds, a soluble

substance, *amylose* (60–80% of the weight of the starch) and an insoluble substance, *amylopectin*, which gelatinizes with hot water. Amylopectin gives little color with iodine, amylose gives a deep blue. Both are hydrolyzed by ferments. It may be that there are a large number of closely related amyloses.

Dextrin, or more properly dextrins, are less complex bodies than starch. The intermediate substances between starch and maltose, formed during digestion, are, in the order of complexity, amylo-dextrins, erythro-dextrins, achroödextrins, and maltodextrins. The first give a blue colour with iodine, the second a red or reddish brown (a mixture of erythro- and amylo-dextrins gives a bluish red colour) while the simpler dextrins give no colour test. Commercial dextrin is prepared from starch by means of heat. It forms a gummy solution which is used for making labels. It is insoluble in alcohol. Most dextrins are precipitated by saturating their solutions with salts, such as ammonium sulphate and sodium sulphate. Most dextrins are precipitated by alcohol when the concentration reaches 75%; the lower dextrins require as much as 90% for precipitation.

The dextrins are dextrorotatory, the (α)D being 192–196° for the higher dextrins. Acid hydrolyzes them to glucose. Diastatic ferments change them to maltose.

Glycogen, $(C_6H_{10}O_5)_x$, resembles dextrin. It is present in animal tissues, mainly in the liver. The liver acts as a storehouse for carbohydrates, storing up in the form of glycogen the sugar which comes to it from the digestive organs, and then reconverting the latter

into sugar as needed by the tissues. A substance has been found in certain vegetables resembling glycogen. Glycogen forms a colloidal solution which is characteristically opalescent. With iodine it gives a reddish brown colour. Its $(\alpha)D$ is $+196.5^\circ$. It hydrolyzes to dextrose. Diastatic ferments form from it dextrins, and finally maltose. It is precipitated by 55% alcohol and by basic lead acetate.

EXPERIMENTS. (1) Test solutions of starch, dextrin, and glycogen with iodine solution.

(2) Test them with lead subacetate solution.

(3) Test them with Fehling's solution before and after hydrolyzing by boiling with dilute HCl.

Gums contain polysaccharides similar to dextrin. *Gum arabic* (acacia) contains arabin ($C_{10}H_{18}O_9?$), which hydrolyzes to arabinose. *Gum tragacanth* contains bassorin.

Agar-agar is a pectin-like substance containing at least seven different carbohydrates, including some starch and cellulose. The most important constituent is gelose, ($C_{24}H_{38}O_{19}?$), which can be hydrolyzed to galactose.

GLUCOSIDES.

Natural glucosides are vegetable substances which can be split up by hydrolysis into a sugar (or sugars) and some other characteristic organic compound or compounds. Many of them are important medicines. A large number of glucosides have been studied. The sugar derived from them is generally glucose.

Phloridzin, $C_{21}H_{24}O_{10}$, is used to produce experimental diabetes in animals. It splits up into glucose and phloretin, $C_{15}H_{14}O_5$ (see also phloroglucin, p. 312).

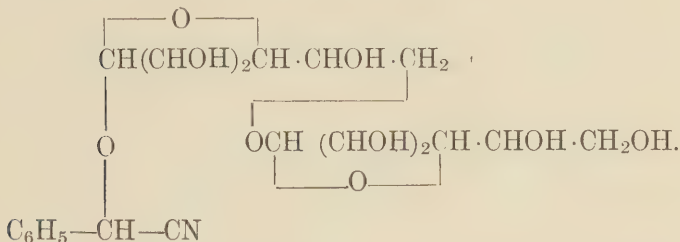
Arbutin, $C_{12}H_{16}O_7$, is a comparatively simple glucoside, hydrolyzing to dextrose and hydroquinone.

Gaultherin, $C_{14}H_{18}O_8$, is a glucoside contained in the wintergreen plant; an accompanying ferment hydrolyzes it to dextrose and methyl salicylate.

Salicin, $C_{13}H_{18}O_7$, is used in medicine; it hydrolyzes to dextrose and saligenin (p. 345).

Amygdalin, $C_{20}H_{27}NO_{11}$, is found in bitter almonds, peach-pits, etc. The ferment emulsin, as well as acids, hydrolyze it to glucose, hydrocyanic acid, and benzaldehyde (see p. 315).

Its structural formula is said to be:



Digitalin, $C_{35}H_{56}O_{14}$, an active principle of digitalis, hydrolyzes to dextrose, digitaligenin, $C_{22}H_{30}O_3$, and digitalose, $C_7H_{14}O_5$.

Digitoxin, $C_{34}H_{54}O_{11}$, the chief active glucoside of digitalis, yields by hydrolysis digitoxigenin, $C_{22}H_{32}O_4$, and digitoxose, $C_6H_{12}O_4$.

Strophanthin, $C_{40}H_{66}O_{19}$, from strophanthus, hydrolyzes to strophanthidin, $C_{27}H_{38}O_7$, methyl alcohol, mannose and rhamnose.

Sinigrin, $C_{10}H_{16}NS_2KO_9$, the glucoside of black mustard, by the action of a ferment present in the mustard splits up into mustard oil, dextrose and $KHSO_4$. In similar manner **sinalbin**, $C_{30}H_{42}N_2S_2O_{15}$, of white mustard yields dextrose, parahydroxytolyl mustard oil and sinapin bisulphate.

Saponins. A large number of glucosides are grouped together into this sub-class. They are non-nitrogenous and form a solution which foams on shaking (*cf.* soaps).

Digitonin is a saponin contained in digitalis, $C_{54}H_{92}O_{28}$; it splits up into digitogenin, $C_{30}H_{48}O_6$, and two molecules each of glucose and galactose.

Artificial glucosides are simpler compounds, for example a methyl glucoside of *d*-glucose has the CH_3 group attached to O of the aldehyde group of glucose.

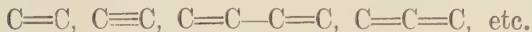
EXPERIMENTS. (1) Try Molisch's test (see p. 250) on a solution of a glucoside.

(2) Hydrolyze some glucoside solution by boiling with dilute H_2SO_4 , neutralize, and examine for sugar with Fehling's solution.

CHAPTER XXI.

UNSATURATED HYDROCARBONS AND THEIR DERIVATIVES.

THE most important unsaturated hydrocarbons are the *ethylenes* and *acetylenes*. Their unsaturation consists in having two or three bonds or linkings between two or more carbon atoms, thus:



Unsaturated substances of this nature readily form addition compounds, as with iodine and bromine. This fact is taken advantage of in analysis of fats and oils, the estimation of the oleic and other unsaturated acids being made by the use of an iodine solution (see p. 178).

Another illustration of the formation of addition compounds is the production of ethylene bromide, $\text{C}_2\text{H}_4 + \text{Br}_2 = \text{C}_2\text{H}_4\text{Br}_2$. Halogen acids (HBr, HI) are added on to these hydrocarbons in similar manner: $\text{C}_2\text{H}_4 + \text{HBr} = \text{C}_2\text{H}_5\text{Br}$. The addition compound is, of course, saturated.

ETHYLENES.

Ethylenes or olefins, C_nH_{2n} , form an homologous series.

Ethylene (ethene, olefiant gas), $CH_2=CH_2$, is the only member of importance, and is contained in coal-gas (about 4%). It is colourless and burns with a yellow flame. Ethylene forms an explosive mixture with oxygen. It is obtained by dehydration of alcohol, as by sulphuric acid (see exp. below): $C_2H_5OH = C_2H_4 + H_2O$.

EXPERIMENTS. (1) In a litre flask heat a mixture of 30 c.c. of alcohol and 83 c.c. of C.P. H_2SO_4 (it is stated that H_3PO_4 can be used instead of H_2SO_4 ,

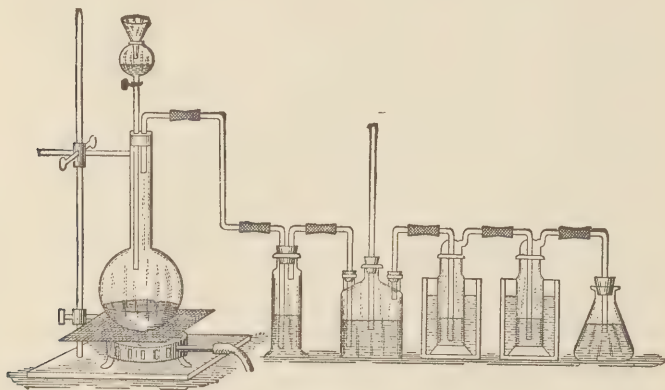


FIG. 24.

avoiding the carbonizing) on a sand-bath. Put a little sand in the flask. Use a three-holed cork. It is best to use rubber stoppers for the entire apparatus because of the pressure of gas which is obtained. In-

sert a dropping funnel, also a thermometer placed so that the bulb is immersed in the liquid. Connect with a series of wash-bottles as shown in the diagram; the first bottle contains H_2SO_4 , the Woulff bottle (having a safety-tube) contains dilute NaOH solution, each of the last bottles contains 10 c.c. of bromine and 10 c.c. of water, finally a *loosely* corked flask containing dilute alkali catches any bromine vapour that may pass over. Begin heating the flask, then when the temperature reaches $170\text{--}175^\circ$ this is maintained thereafter. At the start raise the safety-tube of the Woulff bottle out of the liquid, and attach a piece of tubing. By means of this tube bubble the evolved ethylene through a mixture of solutions of potassium permanganate and sodium carbonate in a test-tube (Von Baeyer's reagent¹) until the pink colour is lost and a brownish precipitate of hydrated manganese dioxide appears. Lower the safety-tube and then begin running slowly into the flask, through the dropping funnel, a mixture of alcohol and sulphuric acid (100 c.c. of the former to 85 c.c. of the latter). Keep up a steady production of ethylene until the bromine is almost decolorized. The bromine bottles should stand in ice-water.

Disconnect the flask and then remove the flame. Wash the ethylene bromide with water in a separating funnel, and finally shake it with NaOH solution. Draw off the bromide into a flask, add dry calcium

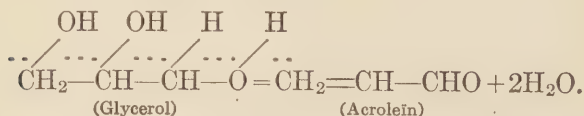
¹ Von Baeyer's reagent is decolorized by formic and hydroxy benzoic acids, by malonic ether, phenols, aldehyde, benzaldehyde, aldehyde bisulphite, acetone, acetophenone, glycerol, and some sugars (because of oxidation of these substances), as well as by unsaturated compounds.

chloride, and cork. After a day or so distil, noting the boiling-point (130.3° , but 129.5° at 730 mm.). Also take the specific gravity (2.1785 at 20°). The bromide is easily solidified, melting at 9.5° .

(2) Bubble coal-gas into Von Baeyer's reagent, as above.

Allyl alcohol (propenol), $\text{CH}_2=\text{CH}\cdot\text{CH}_2\text{OH}$, is an unsaturated alcohol corresponding to the hydrocarbon propene, $\text{CH}_2=\text{CH}\cdot\text{CH}_3$. Its radicle, C_3H_5 , is called *allyl*. This alcohol can be made from glycerol.

Acrolein (acrylic aldehyde), $\text{CH}_2=\text{CH}\cdot\text{CHO}$, is the aldehyde from the above alcohol. It is produced from glycerol (see p. 176):



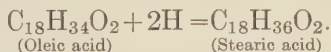
EXPERIMENT. In a dry test-tube mix 4 c.c. glycerol and 0.3 c.c. of 85% phosphoric acid. Fit the tube with a stopper and bent delivery tube. Dip the end of this tube in 2 c.c. of water in a small test-tube. Heat the glycerol to a high temperature. Finally test the solution for reducing power and with Schiff's reagent (aldehyde tests).

By oxidation it becomes **acrylic acid**, $\text{CH}_2=\text{CH}\cdot\text{COOH}$.

Crotonic acid, $\text{CH}_3\cdot\text{CH}=\text{CH}\cdot\text{COOH}$, and **methyl-crotonic acid** (tiglic acid), $\text{CH}_3\cdot\text{CH}=\text{C} \begin{smallmatrix} \text{COOH} \\ \text{CH}_3 \end{smallmatrix}$, are found in croton oil.

Oleic acid is a member of the acrylic acid series. It has the formula, $\text{CH}_3(\text{CH}_2)_7\text{CH}=\text{CH}(\text{CH}_2)_7\text{COOH}$. It

is contained in combination with glycerol as glyceryl trioleate, in many oils, as in olive oil and whale oil, and in animal fats. Oleic acid forms crystals, melting at 14° . Hydriodic acid converts it into stearic acid; this is brought about by addition of hydrogen, thus:



Fusion with caustic potash results in the formation of palmitic and acetic acids.

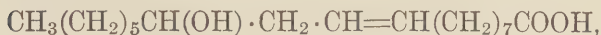
EXPERIMENTS. (1) Dissolve two drops of oleic acid in a few cubic centimetres of ether in a test-tube; shake with a little Von Baeyer's reagent (see p. 270).

(2) Shake some ether with a little bromine water; the ether becomes yellow. Add a few drops of oleic acid and shake. The bromine is taken up, so that the colour is lost.

Erucic acid, $\text{CH}_3(\text{CH}_2)_7 \cdot \text{CH}=\text{CH}(\text{CH}_2)_{11}\text{COOH}$, is present in some oils, as cod-liver oil.

Linoleic acid, $\text{C}_{17}\text{H}_{31} \cdot \text{COOH}$, is believed now to be an acid somewhat similar to oleic acid, but it has two double linkings instead of one. Its molecule takes up four Br atoms, producing tetrabromstearic acid. Its glyceryl ester is contained in linseed oil. It has the power of taking up oxygen from the air, and becoming a hard solid substance, hence its use in paints.

Ricinoleic acid,



is present in castor oil in combination with glycerol.

Allyl sulphide, $(\text{C}_3\text{H}_5)_2\text{S}$, is contained in oil of garlic. It has a disagreeable odour.

Allyl isothiocyanate, $\text{C} \begin{smallmatrix} \diagup \text{N} \\ \diagdown \text{S} \end{smallmatrix} \text{---C}_3\text{H}_5$, is a mustard oil.

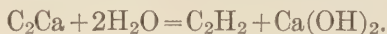
It is contained in glucosidal combination in black mustard and horse-radish.

Allyl thiourea (allyl sulphocarbamide, thiosinamine), $\text{S}=\text{C} \begin{smallmatrix} \diagup \text{NH}_2 \\ \diagdown \text{NH} \cdot \text{CH}_2 \cdot \text{CH}=\text{CH}_2 \end{smallmatrix}$, is used as a remedy.

ACETYLENES.

These hydrocarbons, $\text{C}_n\text{H}_{2n-2}$, form a series of which few members are known.

Acetylene, $\text{CH}\equiv\text{CH}$, is the only important member. Small quantities are synthesized directly from carbon and hydrogen when a stream of hydrogen is passed between the carbon poles of an electric arc-light, a small quantity of methane being formed at the same time. It is formed when a Bunsen burner "snaps back." The gas is made most easily and cheaply by the action of water on calcium carbide,



When used with a special burner it gives a brilliant light. It is used extensively as an illuminating gas. It is a colourless gas of unpleasant odour.

EXPERIMENTS. (1) Put 10 gm. of calcium carbide in a dry flask or bottle, cork with a two-holed cork. By one hole suspend a dropping funnel containing water, into the other hole fit a bent delivery tube. Let the water drop on the carbide very slowly. Bubble the acetylene into Von Baeyer's reagent until the test is

secured. Then connect with a platinum-tipped glass tube such as is used for burning hydrogen. Light the acetylene—a brilliant flame is obtained.

(2) Test the acetylene by inverting a beaker which is moistened inside with a solution of cuprous chloride in ammonia over the stream of gas—a red precipitate of copper acetylide, C_2Cu_2 , is formed.

Repeat the experiment, causing a Bunsen burner to strike back, thus producing acetylene.

The cuprous chloride is easily prepared as follows: dissolve 0.5 g. of copper sulphate in a little water, add 2 c.c. of concentrated ammonium hydroxide, then 1.5 g. hydroxylamine hydrochloride and dilute to 25 c.c.

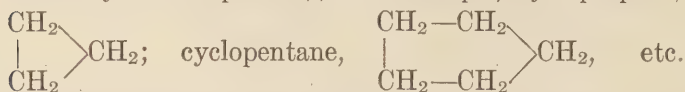
CHAPTER XXII.

CYCLIC AND BICYCLIC COMPOUNDS.

THESE form a transitional group between the fatty and the aromatic compounds. They contain one or two closed carbon chains, differing from typical aromatic compounds in that their C atoms either have their full valence obviously satisfied (saturated) or have a double linking which causes the compound to respond to the tests for unsaturation (cf. benzene, p. 285).

CYCLIC COMPOUNDS.

Certain hydrocarbons with the general formula C_nH_{2n} have properties quite different from those of the ethylene series; indeed, they behave quite like members of the methane series. Thus, they do not reduce Von Baeyer's reagent. Therefore, instead of representing them as composed of an open chain with double linkings, their formulæ are written as closed chains (and hence they are called cyclic compounds); for example, cyclopropane,



They are given the same names as the members of the methane series, with the prefix *cyclo*. Certain of these cyclic compounds have been found in Caucasian petroleum.

Cycloses. There are a number of hydroxy derivatives of the cyclic hydrocarbons; these are cyclic alcohols or cycloses (OH attached to C of the ring). The most important of these is inosite.

Inosite, $C_6H_{12}O_6$, hexahydroxycyclohexane, has the same empirical formula as the hexoses; it is not a sugar, however. It occurs in animal tissues and in urine, being from this source optically inactive; *d* and *l* and *dl* varieties of inosite are said to occur in plants.

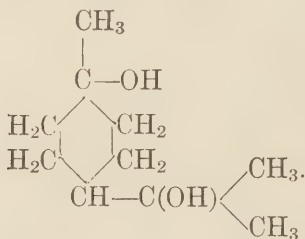
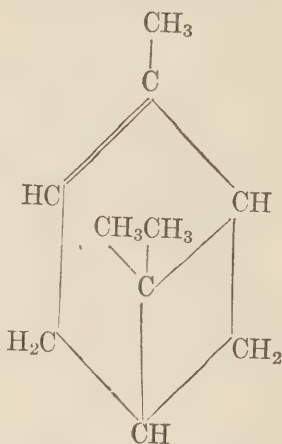
BICYCLIC COMPOUNDS. TERPENES AND CAMPHORS.

In the volatile oils obtained from coniferous trees (and in various other natural products) are contained hydrocarbons having the empirical formula $C_{10}H_{16}$. These are called terpenes. They decolorize Von Baeyer's reagent (see p. 270), and they combine directly with one or two molecules of HCl. They therefore possess the general properties of unsaturated compounds, but yet they differ from these in many respects and may be considered to belong to the class of cyclic compounds since they contain a closed chain of carbon atoms. By mild oxidation many of them can be converted into cymene (paramethylisopropyl benzene) (see p. 297) and by further oxidation into paratoluic acid (see p. 323), both of these substances being aromatic compounds.

The terpenes and camphors include many bodies of medical and commercial value, and of these the following are important:

1. **Pinene**, $C_{10}H_{16}$, the principal constituent of oil of turpentine, has the structural formula annexed

and exists as stereoisomers. It is dextrorotatory. Its boiling-point is 155° . When combined with hydrochloric acid it forms pinene hydrochloride, $C_{10}H_{17}Cl$, which, since it resembles camphor, is known as *artificial camphor* (see exp. below). Artificial camphor can be converted into true camphor. *Oil of turpentine* is obtained by incising the bark of fir-trees: the crude oil contains, in addition to turpentine, which is separated by distillation, residues constituting rosin. By destructive distillation or by steam distillation of resinous waste wood (pine and fir) are obtained wood turpentine and pine oils. Pinene can be converted by alcohol and nitric acid into **terpin hydrate**, which is a crystalline substance used in medicine. It is not bicyclic like pinene. Its formula is

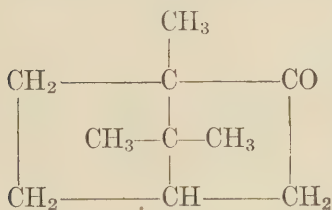


EXPERIMENTS. (1) Prepare artificial camphor. Into 10 c.c. of freshly distilled turpentine that is free of water (treat with calcium chloride before distilling)

contained in a flask kept cool by a freezing-mixture, bubble dry HCl gas until crystals of pinene hydrochloride appear. Make the HCl by heating in a retort a mixture of dried NaCl and C.P. H_2SO_4 . Collect the crystals on a filter and examine them.

(2) Shake some turpentine with Von Baeyer's reagent. Is there evidence of unsaturated linking?

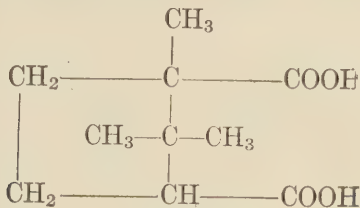
2. **Camphor**, $\text{C}_{10}\text{H}_{16}\text{O}$. This is a gum obtained by distilling with steam the finely chopped wood of the camphor tree. Its chemical structure has recently been worked out, and it is now produced by synthetic processes on a commercial scale. Camphor contains



a ketone group, so that it may be called a terpene ketone having the formula as shown opposite. In solution it is dextrorotatory.

Borneol is a secondary terpene alcohol corresponding to camphor, it has CHOH instead of the CO group.

Carvacrol (isomeric with thymol) can be obtained

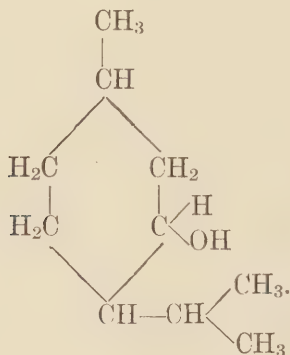


(*Camphoric acid.*)

from it by the loss of two atoms of hydrogen. By warming with phosphorus pentoxide it is converted into cymene. It melts at 176.4° , and sublimes, the

sublimate forming crystals. *Hydroxycamphor* (oxycamphor) has a secondary alcohol group in the place of a CH_2 group of camphor. It is one of the newer remedies. *Camphor monobromide* is $\text{C}_{10}\text{H}_{15}\text{BrO}$. Camphor can be oxidized to *camphoric acid* (see formula on page 278).

3. **Menthol** is a terpene alcohol containing a secondary alcohol group CHOH . Its formula is given below. Like camphor, it contains no unsaturated linkings. Menthol is a white crystalline substance melting at 42° , and is the chief constituent of oil of peppermint. Its solution is laevorotatory. It is useful as a medicine. It is excreted in combination with glycuronic acid (p. 204).



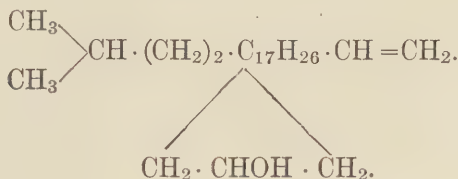
Sandalwood oil contains two isomeric unsaturated primary alcohols, one being bicyclic and the other tricyclic. They have the formula, $\text{C}_{15}\text{H}_{24}\text{O}$.

Polyterpenes have two or more terpene rings.

SUBSTANCES ALLIED TO TERPENES.

Caoutchouc or **rubber** contains a terpene-like substance, $C_{30}H_{68}O_{10}$. This is decomposable into $3(C_{10}H_{16}) + 10H_2O$. Rubber is the hardened milky juice of certain tropical plants. **Gutta-percha** is similar to rubber.

Cholesterol (cholesterin), $C_{27}H_{46}O$, is an important constituent of bile. It is also present in egg yolk, cod liver oil and lanolin. It belongs to a class of compounds called *sterins*, which includes also ischolesterol, koprosterol, phytosterol and other substances. It has an unsaturated linking and a secondary alcohol group:



The portion $C_{17}H_{26}$ is believed to be related to the polyterpenes. Its crystalline form is characteristic. It melts at $145\text{--}146^\circ$. In ether solution it is lævorotatory.

Koprosterol, $C_{26}H_{46} \cdot \text{CHOH}$, is a similar compound occurring in the fæces.

Phytosterol is of vegetable origin, being most abundant in leguminous seeds and in vegetable oils. It can be detected and distinguished from cholesterol by the fact that its ester with acetic anhydride has a higher melting-point (125°) than the similar ester from cholesterol (114.5°).

CHAPTER XXIII.

THE AROMATIC HYDROCARBONS.

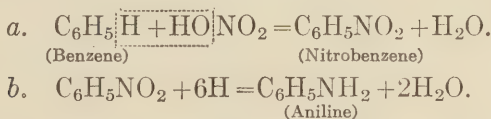
NEARLY all of the substances which we have so far studied are represented in their formulæ as composed of open chains of carbon atoms. A few of them, such as the anhydrides of hydroxy-acids, lactones, and the purin derivatives, have to be represented as composed of closed chains. It is only in the case of the aromatic bodies and the cyclic compounds, however, that each link in the closed chain is represented by a C atom. In connection with the paraffin derivatives containing closed chains, moreover, it will be remembered that their closed chain is readily opened, e.g., an anhydride of an acid can easily be converted into the corresponding acid, etc.

We come now to a group of organic substances—the largest group, indeed—the members of which are composed of closed chains that cannot readily be opened. In the older chemical nomenclature the bodies belonging to this group were called aromatic bodies on account of the presence of an agreeable aroma, and by this name they are still known. They may all be looked upon as derivatives of a substance called benzene, C_6H_6 , just as all the fatty substances may be represented as

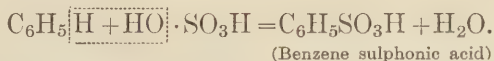
derivatives of methane. Many of the derivatives of benzene are indeed quite analogous with those of methane, undergoing similar reactions and possessing much the same properties. Unlike the fatty series, few of them are useful as foods; many of them, however, have very pronounced physiological actions. Commercially they are of very great value.

There are four simple reactions in which the two groups—i.e., the aromatic and the fatty—give very different results:

1. With concentrated nitric acid the aromatic hydrocarbons readily form nitro compounds, which on reduction with nascent hydrogen yield amino-derivatives. Paraffins are unaffected by HNO_3 .



2. With concentrated sulphuric acid they form sulphonic acids (see p. 193). Paraffins are unaffected by H_2SO_4 .



3. Chlor- and brombenzene are very stable and do not readily react with KOH , whereas in the case of methyl chloride, etc., hydroxyl can readily be substituted for the Cl (see p. 113).

4. When a benzene substitution product with one or more side chains of carbon atoms is oxidized, the side chain or chains become oxidized in such a way as to form simply carboxyl.

BENZENE.

At the outset we must study the structure of benzene, since, as has been noted, this is the mother substance of the aromatic bodies. We must furnish evidence that its formula is correctly represented as having a closed chain.

Benzene ¹ (benzol), C_6H_6 . When coal is heated in gas retorts, in the preparation of artificial gas, there passes out with the gas a vapour which is condensed in specially arranged condensers. The condensed vapours constitute coal-tar. The ammonia and pyridine bases which are also given off from the retorts are dissolved in water. The tar is a mixture of neutral, acid, and a small quantity of basic bodies, and also contains particles of carbon in suspension (hence its blackness). The tar products are separated, partly by fractional distillation and partly by chemical means. The crude tar is distilled into four fractions, as follows:

- (1) Light oil (fraction up to 170°).
- (2) Carbolic oil (170° – 230°).
- (3) Heavy or creosote oil (230° – 270°).
- (4) Anthracene oil (above 270°).

The residue contains a large amount of carbon.

The light oil is purified by treatment with acid and with alkali and is then distilled. It is in the light oil that most of the benzene and its homologues are contained. The benzene can be further purified by fractional distillation, then by treatment with concentrated H_2SO_4 to remove thiophene (C_4H_4S), and finally by freezing it and pouring off the liquid portion.

¹ Different from benzine (see p. 98).

Benzene may also be obtained (1) by distillation of a salt of an aromatic acid with soda-lime, a reduction which, it will be remembered, is analogous with that employed for the preparation of methane:



(2) By passing acetylene (C_2H_2) through a red-hot tube. This method illustrates how synthesis of aromatic out of fatty hydrocarbons can be accomplished.

(3) By heating potassium in a current of CO. A synthesis occurs resulting in the formation of $\text{C}_6(\text{OK})_6$, potassium carbonyl. This is a derivative of benzene and can be converted into benzene by distillation with zinc dust in the presence of water.

Benzene is a colourless liquid of aromatic odour, boiling at 80.3° (corrected) (at 80.12° at 757.3 mm.). Its melting-point is 5.4° . Its specific gravity is 0.8736 at $\frac{20^\circ}{4^\circ}$. Benzene is inflammable and immiscible with water. It is a good solvent for many substances. It can be used for molecular weight determinations (see p. 52).

EXPERIMENTS. (1) Mix thoroughly 25 gm. of benzoic acid and 50 gm. of powdered quicklime, and put into a dry retort (*cf.* preparation of methane, p. 97). Connect with a condenser and heat gradually. Treat the distillate with dry calcium chloride and redistil from a small fractionating flask (an air-condenser will do). Note the boiling-point. Put the distillate into a dry test-

tube and cool in a freezing-mixture until crystallization occurs. Remove from the mixture and warm the test-tube with the fingers while stirring the crystals with a thermometer. At what point does the temperature remain constant while the crystals are melting?

(2) Determine the specific gravity of some pure benzene at 15° with the Westphal balance.

(3) Shake a few cubic centimeters of benzene with Von Baeyer's reagent. Does it act like an unsaturated compound?

Structure of Benzene. From its empirical formula, C_6H_6 , one would expect to find benzene giving reactions like those of acetylene or other unsaturated hydrocarbons,¹ that is to say, reactions indicating the existence of double bonds between the carbon atoms. Such, however, is not the case. Benzene does not readily combine with halogens, i.e., form addition products; it is not sensitive toward oxidizing agents; it does not decolorize a solution of potassium permanganate containing sodium carbonate. Unsaturated compounds readily give all these reactions. It is evident, therefore, that the formula for benzene cannot be represented as containing double bonds between the carbon atoms. Further, the formula must represent all the hydrogen atoms as simi-

¹ Cf. dipropargyl, C_6H_6 , $CH\equiv C-CH_2-CH_2-C\equiv CH$. This has a distinctly greater heat of combustion than benzene, therefore the kind of linking that we have in benzene must be quite different from that in ordinary unsaturated compounds.

larly combined with the carbon atoms, *for there are no isomers of the monosubstitution products of benzene*: there is only one monobrombenzene, one monochlorbenzene, etc. This important fact can be shown in a variety of ways. Perhaps the simplest is as follows: If we treat benzene with bromine one of the six hydrogen atoms is replaced by bromine. Numbering the hydrogen atoms

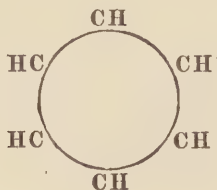
thus: $\overset{1}{\text{H}} \overset{2}{\text{H}} \overset{3}{\text{H}} \overset{4}{\text{H}} \overset{5}{\text{H}} \overset{6}{\text{H}}$, let us suppose that $\overset{1}{\text{H}}$ is replaced. Our problem is to see whether the monobrombenzene thus formed is identical with that formed by replacement of $\overset{2}{\text{H}}$, $\overset{3}{\text{H}}$, etc. To do this we must replace another

H in the compound $\text{C}_6 \overset{1}{\text{Br}} \overset{2}{\text{H}} \overset{3}{\text{H}} \overset{4}{\text{H}} \overset{5}{\text{H}} \overset{6}{\text{H}}$ by some group which can then be substituted by Br, the Br originally present being meanwhile replaced by H. This can be accomplished by treating monobrombenzene with nitric acid, the resulting compound having the formula $\text{C}_6\text{H}_4\text{BrNO}_2$. For the sake of argument, let us suppose that $\overset{2}{\text{H}}$ is replaced by the NO_2 group, thus:

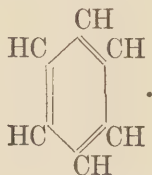
$\text{C}_6 \overset{1}{\text{Br}} \overset{2}{\text{NO}_2} \overset{3}{\text{H}} \overset{4}{\text{H}} \overset{5}{\text{H}} \overset{6}{\text{H}}$. By the action of nascent H the NO_2 group becomes an amido group, NH_2 (see p. 329), and the Br is replaced by H. The formula for our substance is then $\text{C}_6\text{H} (\text{NH}_2) \overset{2}{\text{H}} \overset{3}{\text{H}} \overset{4}{\text{H}} \overset{5}{\text{H}} \overset{6}{\text{H}}$. (aniline). By treating a salt of aniline (p. 334) with nitrous acid the diazonium salt is formed, which by treatment with hydrobromic acid (see p. 335) yields a monobrombenzene in which the Br atom stands in place of $\overset{2}{\text{H}}$, and yet this is found to be identical in properties with that monobrombenzene in which Br was in place of $\overset{1}{\text{H}}$. By similar reactions the various H atoms may be replaced one by

one, the resulting monosubstitution product being always the same.

This fact makes it evident that we cannot represent the C atoms as linked together in an open chain, for then there would necessarily be two or three varieties of monosubstitution products, depending upon the particular C atom in the chain to which the substituting group is linked (*cf.* alcohols, p. 87). On this account Kekulé, who had been a mechanical engineer before he became a chemist, conceived the notion that the C atoms must be represented as forming a ring, and that the formula for benzene must be



or, as it is more usually written,



To satisfy the quadrivalence of the C atom, it is necessary, as shown in the second formula, to assume that certain of these bonds are double. We have, however, seen that

when double bonds between carbon atoms exist, the resulting body is unsaturated. To explain this apparent inconsistency, Kekulé supposes that in benzene there are really no double bonds in the same sense as they exist in unsaturated hydrocarbons, but that the double bond is *dynamic*, changing about from place to place, and is really unrepresentable in a formula.¹

Collie has made an extremely interesting suggestion as to the spatial relations of the C atoms in benzene. His model represents each C atom as at the centre of a tetrahedron, and neighbouring carbons are attached by bands, while an H atom is attached to each C through the centre of a face not at an angle of the tetrahedron. The rest of the model is mechanical serving for support of the figure (p. 289).

Such an arrangement permits rotation of two kinds, (1) the tetrahedra can rotate on their own axes simultaneously, and (2) the three pairs of tetrahedra can rotate on the axes passing through the centre of the model. This possibility of double rotation conforms very well to the idea that the benzene molecule must be conceived as a system in vibration. By those rotations the model can be made to correspond successively to the following formulæ:

¹ The centric formula  has been proposed to indi-

cate pictorially this self-saturation of the carbon atoms of the ring without definite extra linkings. This formula also has the advantage of emphasizing the distinguishing difference of all aromatic from other organic compounds.

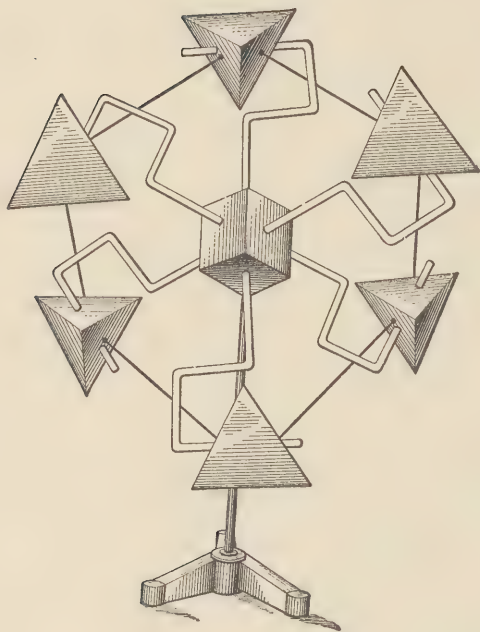
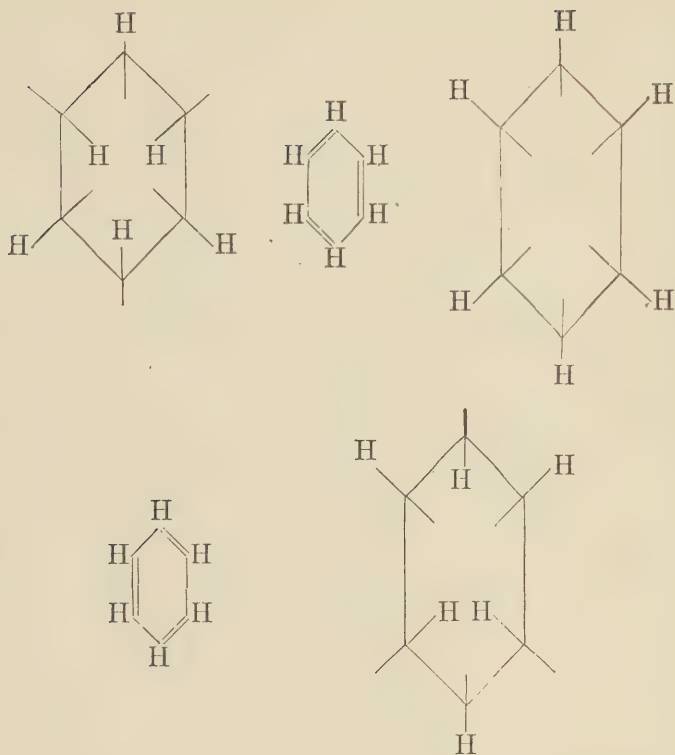
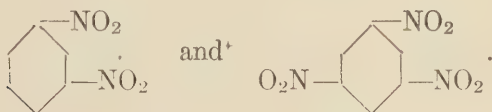


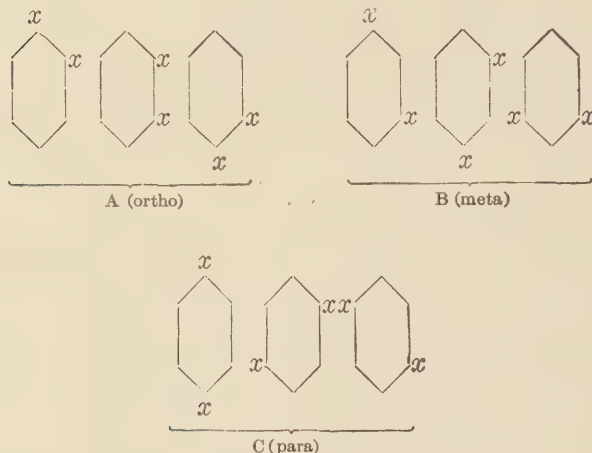
FIG. 25.



The first and last would indicate that there are two sets of H atoms. Possibly this explains why, in the substitution of certain groups for H, there is a tendency to displace alternate H atoms instead of successive ones, for instance nitric acid forms



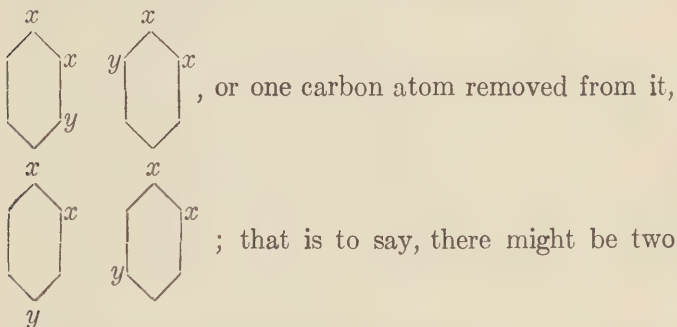
In perfect harmony with this conception of a ring is the fact that there are *three kinds of disubstitution products*. That three and only three are possible will be evident from the following formulæ, where x represents some substituting group:



The substituting groups may replace neighbouring hydrogens, as in the formulæ marked A; or be so arranged that a carbon of the ring intervenes, as in B; or with two such atoms intervening, as in C. Bodies exhibiting the first arrangement are called *ortho*, the second *meta*, and the third *para*.¹ For certain of the simple disubstitution products of benzene it has been definitely established which is *ortho*, which *meta*, and which *para*. To ascertain to which of these groups an unknown substance belongs it is necessary to transform it into

¹ The abbreviations *o*, *m*, and *p*, are used for these terms.

one of the known simpler forms, it being considered that the unknown substance contains the same arrangement of its side chains as does the simpler substance which it yields. It remains for us to see, therefore, how it is possible to tell to what class some simple disubstitution product of benzene belongs. This is done by a study of the number of isomeric compounds which can be produced by substituting still another hydrogen atom of the ring by a group different from the other two groups. Suppose *y* to represent this third substituting group. In an *ortho* compound we might have *y* attached next to *x*,



trisubstitution products which on removal of *y* would yield the same disubstitution product. In a *meta* compound *y* might occupy three positions which would be different; thus, between the two *x*'s as in A, or beyond but next to them as in B, or separated from them by carbon atoms of the ring as in C, thus:



A



B



C

That is to say, there are three trisubstitution products which yield the same disubstitution product. In a *para* compound *y* could occupy only one position, i.e., next to an *x*; therefore there is only one trisubstitution product that could be converted into it, thus:



. To take an example: There are six diamino-

benzoic acids with the formula $C_6H_3 \begin{matrix} \swarrow NH_2 \\ \rightarrow NH_2 \\ \searrow COOH \end{matrix}$.

By removal of the carboxyl group three of these yield diaminobenzenes which are identical in properties (melting-point 63°), and which must therefore be meta; two others yield another variety of diaminobenzene (melting-point 102°) which must be ortho; and the remaining one yields yet another diaminobenzene (melting-point 140°) and which is para.

For convenience of description it is customary to number the carbon atoms in the benzene ring thus:



When three similar groups (e.g., three hydroxyls) are attached to the benzene ring, only three isomers are possible, *symmetrical* (positions 1, 3 and 5), *unsymmetrical* (1, 3, 4) and *adjacent* (1, 2, 3).

Analogous to the alkyl radicles of paraffin hydro-

carbons is the phenyl group, C_6H_5 . This is sometimes designated by the Greek letter ϕ .

HOMOLOGUES OF BENZENE.

The chief homologues of benzene are toluene, $C_6H_5 \cdot CH_3$, the xylenes, $C_6H_4(CH_3)_2$, mesitylene, $C_6H_3(CH_3)_3$, and durene, $C_6H_2(CH_3)_4$.

Toluene (toluol), $C_6H_5 \cdot CH_3$, boiling-point 111° , specific gravity 0.8656 at $\frac{20^\circ}{4^\circ}$, can be separated from light oil or can be prepared synthetically by treating a mixture of monobrombenzene and methyl iodide with sodium (*cf.* synthesis of paraffins, p. 95):



This reaction clearly illustrates its structure as methyl benzene. By oxidation the CH_3 group becomes carboxyl, *benzoic acid*, C_6H_5COOH , being therefore formed.

Xylenes, $C_6H_4(CH_3)_2$. Being disubstitution products of benzene, there are three of these. The boiling-point of ortho is 141.9° , meta 139.2° , para 138° ; the specific gravity at $\frac{20^\circ}{4^\circ}$ of ortho is 0.8766, meta 0.8655, para 0.8635. The xylenes can be prepared from light oil. By

oxidation they give first *toluic acids*, $C_6H_4 \begin{cases} CH_3 \\ COOH \end{cases} \begin{cases} o \\ m, \\ p \end{cases}$

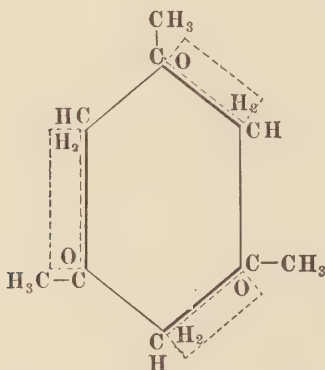
and then *phthalic acids*, $C_6H_4 \begin{cases} COOH \\ COOH \end{cases} \begin{cases} o \\ m. \\ p \end{cases}$. The xylol,

which is extensively used in histological work and as a fat-solvent, is a mixture of the xylenes.

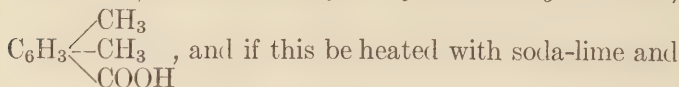
Isomeric with the xylenes is **ethyl benzene**, $C_6H_5 \cdot C_2H_5$, which on oxidation yields benzoic acid, C_6H_5COOH , instead of toluic or phthalic acid.

Mesitylene, $C_6H_3(CH_3)_3$, boiling-point 164.5° , specific gravity 0.8694 at $\frac{9.8^\circ}{4^\circ}$, is also contained in light oil,

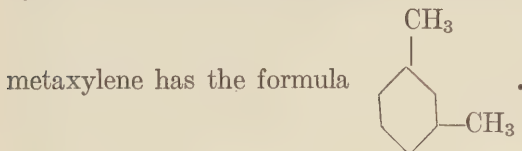
and can likewise be obtained by a most interesting and important synthesis, viz., by distilling a mixture of acetone and sulphuric acid (see exp. below). Three acetone molecules no doubt enter into the synthesis, the sulphuric acid removing a molecule of water from each and causing them to condense together into a ring as represented in the following formula.



Mild oxidation of mesitylene yields *mesitylenic acid*,



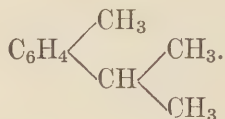
the COOH group be thus removed (see p. 284), metaxylene is obtained, furnishing corroborative proof that



EXPERIMENT. *Preparation of a benzene hydrocarbon (mesitylene) from a fatty compound (acetone).* Into a 500 c.c. flask put 100 gm. of clean sand, 50 c.c. of acetone, and a cooled mixture of 65 c.c. of C.P. H_2SO_4 and 30 c.c. of water. Mix thoroughly and allow to stand for at least two days. Filter with the aid of suction, using a hardened filter paper. Distil, using an oil-bath. Shake the distillate with dilute alkali, then with water. Separate the oily layer, dry it with calcium chloride, and distil. Collect the fraction coming over above 150° . Notice the aromatic odour. Test it as follows: Place a few small crystals of anhydrous aluminium chloride in a dry test-tube; heat gradually until a thin coating of sublimate is secured in the upper part of the tube. When cool add a solution of a few drops of the mesitylene in about 2 c.c. of chloroform and cork the tube. Most aromatic hydrocarbons and some of their derivatives give a colour reaction under the conditions of this test, at least on standing.

Durene is of on importance.

Cymene is paramethylisopropyl benzene,



It can be obtained by warming camphor, $\text{C}_{10}\text{H}_{16}\text{O}$, with phosphorus pentoxide, or by treating pinene, $\text{C}_{10}\text{H}_{16}$ (from turpentine), with chlorine. It is a constituent of certain ethereal oils, as oil of *eucalyptus* and oil of *thyme*.

CHAPTER XXIV.

AROMATIC HALOGEN DERIVATIVES.¹

Of Benzene. As already explained, there is only one kind of monohalogen substitution product of benzene. *Chlor- and brombenzene* can be prepared by treating benzene with chlorine or bromine. *Iodobenzene* is prepared with greater difficulty, it being necessary to have an oxidizing agent present (I_2 or Fe_2Cl_6). By prolonged action more than one hydrogen atom of the benzene molecule becomes replaced by the halogen, and of course there are *o*-, *m*-, and *p*-disubstitution products; indeed, all the H atoms may be replaced, hexachlor- (or brom-) benzene being formed, C_6Cl_6 (or C_6Br_6). If the reaction takes place in direct sunlight, addition products, instead of substitution products, are obtained, such as $C_6H_6Cl_6$ and $C_6H_6Br_6$. These readily decompose into the halogen acid and trisubstitution products of benzene:



¹ It will be advisable for the student to look over the synopsis of aromatic compounds (p. 380) frequently in studying the following pages.

In contrast to the halogen derivatives of the paraffins, the halogen substitution products of benzene are very stable and do not readily give up their halogen atoms to be replaced by hydroxyl, a cyanide group, an amido group, etc., as alkyl halides do.

Of Toluene. There are four bodies with the empirical formula C_7H_7Cl . One of these, called *benzyl chloride*, has a very disagreeable odour and readily yields up its Cl atom when heated with hydroxides, cyanides, etc. It behaves in this respect like a fatty derivative. These facts suggest that the Cl atom is in the side chain, thus $C_6H_5CH_2Cl$. That this is really so is proven by the fact that when oxidized it yields benzoic acid, C_6H_5COOH . It is formed when toluene is treated at boiling temperature or in direct sunlight with the halogen.

The other three bodies are called *chlortoluenes* and have agreeable aromatic odours. They do not give up their Cl atom when heated with hydroxides, etc. They behave in this respect like chlorbenzene, so that the Cl atom must be present in direct connection with the benzene nucleus itself, thus: $C_6H_4 \begin{smallmatrix} \diagup CH_3 \\ \diagdown Cl \end{smallmatrix}$. The three varieties are ortho, meta, and para. When oxidized the Cl atom is not removed, but the CH_3 side chain becomes converted into $COOH$, a substituted benzoic acid being thus formed, i.e., a chlorbenzoic acid. They are prepared by treating toluene in the cold, and in diffused light, with chlorine, the reaction being greatly accelerated by the presence of antimony trichloride or some other halogen-carrier.

In the same way with the di- and trihalogen substi-

tution products of toluene, substitution may occur either in the phenyl¹ or methyl groups. The other substitution products of toluene exhibit a similar isomerism.

¹ Phenyl is the name given to the radicle C_6H_5 .

CHAPTER XXV.

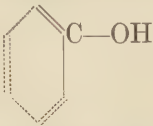
AROMATIC HYDROXY COMPOUNDS.

ONE or more of the H atoms of benzene may be displaced by a hydroxyl group —OH , the resulting body being called a phenol. Phenols manifest faintly acid properties, so that some of them are called acids; thus, monohydroxybenzene is carbolic acid, and trihydroxybenzene, pyrogallie acid. Their acidity indicates that in solution a few H^+ ions are liberated. Compare the acid power of phenol with that of weak organic acids, as shown in the table (appendix, p. 409). When brought into contact with alkaline hydroxides, salts, called phenolates or phenoxides, are formed, e.g., $\text{C}_6\text{H}_5\text{ONa}$, sodium phenolate. Such phenolates can be obtained by dissolving the phenol in a solution of the hydroxide and evaporating to dryness. They are, therefore, stable in the presence of water and thus differ from the alcoholates, which are decomposed by water and can be formed only by acting on alcohol with the alkali metals. By union with phenyl, therefore, the hydroxyl group —OH comes to possess quite different properties than when it is combined with a paraffin (see p. 113).

On the other hand, even such weak acids as carbonic (H_2CO_3 or $\text{CO}_2 + \text{H}_2\text{O}$) are more strongly acid than

phenol and can decompose phenolates, liberating the phenol. The percentage dissociation for a decinormal solution of phenol is only 0.0037, that of carbonic acid being 0.174.

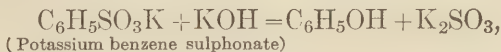
In other respects phenols behave like tertiary alcohols

(cf. tertiary alcohol group $\begin{array}{c} | \\ -\text{C}-\text{OH} \\ | \end{array}$ with  of

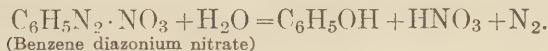
phenol), thus: they form ethers and ethereal salts, but do not yield aldehydes, ketones, or acids on oxidation (see p. 90). The OH group can be removed by treatment with PCl_5 . Using the same classification as for alcohols, we may, therefore, subdivide them into mon-, di-, and triacid phenols.

MONACID PHENOLS.

Phenol (carbolic acid), $\text{C}_6\text{H}_5\text{OH}$. This important substance is extracted from the carbolic oil fraction of coal-tar by shaking with a solution of alkali, the carbolic acid in the resulting solution being then precipitated by sulphuric acid and redistilled (see exp. below). It may also be prepared by fusing potassium benzene sulphonate with caustic potash:



or by boiling a diazonium salt with water (see p. 335):

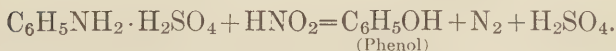
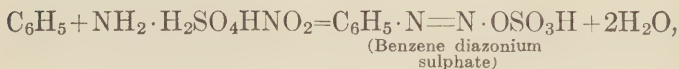
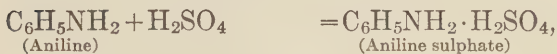


EXPERIMENTS. (1) Extract phenol from heavy oil (carbolic oil) in the following manner: Dissolve 2 c.c.

in ether, add 10 c.c. of 5% NaOH and shake for five minutes. Draw off the bottom layer with a pipette and filter through a wet filter. Acidulate the filtrate with HCl, cool and shake with ether vigorously. Remove the ether layer with a pipette, transferring it to an evaporating dish. Evaporate on a steam bath away from a flame. Note the odour of the residue and test it for phenol (see tests, 3).

(2) *Prepare phenol from aniline.* Into a freshly made (hot) solution of 12 c.c. of C.P. H_2SO_4 in 50 c.c. of water put 10 c.c. of aniline, allowing it to flow down the wall of the beaker. Mix well and dilute with 100 c.c. of water. Cool with running water, then add sodium nitrite solution (8.5 gm. in 40 c.c. of water) until a drop of the mixture well diluted gives a blue colour to starch-potassium-iodide paper (soak filter-paper in boiled starch solution containing potassium iodide, dry it, and cut up into strips), showing the presence of free nitrous acid. This procedure is called *diazotizing*, because the nitrous acid changes the aniline salt into a diazonium salt. Transfer to a half-litre flask, heat to 40° – 50° in a water bath for half an hour, then distil with steam (see p. 15). The phenol passes over into the condenser with the steam. Saturate the distillate with sodium chloride and shake with several small portions of ether. Dry the separated ethereal extract over dehydrated sodium sulphate for several days in a corked flask. Distil off the ether (away from a flame if possible, a steam-bath is safest); finally draw a stream of air through the hot flask with a suction-pump. Distil the phenol, using an air-condenser. Collect the phenol by fractions, testing the first fractions

as in (3) below. When a drop of distillate on cooling with water, crystallizes, collect samples.



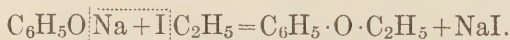
(3) *Tests.* (a) To half a test-tube of phenol solution add bromine water until a white precipitate of *tribromphenol* forms. (b) Test some solution with a drop of ferric chloride solution—a violet colour. (c) To a few cubic centimetres of solution add Millon's reagent and boil—a red colour or precipitate. (d) To 10 c.c. of phenol solution add a few cubic centimetres of ammonia, then small portions of bleaching-powder, shaking after each addition, until a blue colour is obtained.

Phenol, when pure, forms colourless rhombic needles melting at 39.6° and boiling at 182.9°. Its specific gravity is 1.039 at 58.5°. It becomes reddish on exposure to light. It dissolves in 20 parts of water at 17°; in other words, by shaking phenol crystals with water and allowing them to stand at room temperature an approximately 5% solution is obtained, and the crystals, by taking up water, will liquefy and form an oily layer at the bottom of the bottle. It mixes with glycerol, alcohol and ether in all proportions. The easiest way to prepare a 5% phenol solution is by dilut-

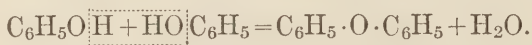
ing the proper quantity of a 50% solution in glycerol. Phenol is extensively used in surgery as an antiseptic. It is produced in the intestine by the action of micro-organisms on the aromatic groups in protein; the phenol thus produced is absorbed into the blood and unites with potassium sulphate, to be excreted into the urine as potassium phenol sulphate, $\text{C}_6\text{H}_5 \cdot \text{OSO}_2\text{OK}$. Phenol uncombined with alkali is poisonous. It is often taken with suicidal intent.

The **derivatives of phenol** are (1) the ethers and ethereal salts and (2) the substitution products.

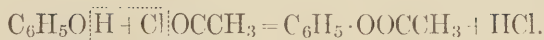
The **ethers** are of two classes: (a) the *aromatic-fatty* ethers, such as phenyl ethyl ether, $\text{C}_6\text{H}_5 \cdot \text{O} \cdot \text{C}_2\text{H}_5$, and (b) the *true aromatic* ethers, such as phenyl ether, $\text{C}_6\text{H}_5 \cdot \text{O} \cdot \text{C}_6\text{H}_5$. The aromatic-fatty ethers may be obtained by allowing an alkyl halide to act on a phenolate.



The chief members of this class are *anisole* (phenyl methyl ether) and *phenetole* (phenyl ethyl ether). They are both liquids having pleasant odours. The true aromatic ethers cannot be prepared by this reaction, since a halogen cannot easily be displaced from phenyl. They may, however, be obtained by heating phenol with a dehydrating agent such as aluminium chloride:



The **ethereal salts**. *Phenyl acetate*, $\text{C}_6\text{H}_5 \cdot \text{OOCCH}_3$, is a type of these and is prepared by the action of acetyl chloride on phenol:

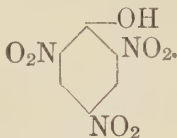


The **substitution products of phenol**. In these one or more hydrogens of phenyl (C_6H_5) are replaced by some radicle but the hydroxyl group remains intact. They form a large class, but only a few of the compounds will be discussed here, the most important of the others being considered later.

Tribromophenol, $\text{C}_6\text{H}_2\text{Br}_3\text{OH}$, is precipitated by treating phenol with bromine water (see exp. above).

Mononitrophenol, $\text{C}_6\text{H}_4(\text{NO}_2)\text{OH}$, may be ortho or para and is prepared by the action of dilute nitric acid on phenol.

Trinitrophenol, $\text{C}_6\text{H}_2(\text{NO}_2)_3\text{OH}$, or **picric acid**, is prepared by allowing strong nitric acid to act on phenol (see exp. below). The NO_2 groups are symmetrically attached to the benzene ring, thus:

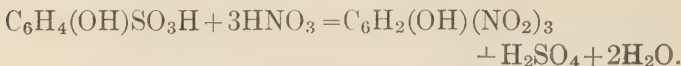


It forms yellow prismatic crystals, has a bitter taste, and is very poisonous. In watery solution it stains silk and wool yellow and is used in histology for staining elastic fibres and also zymogen granules in gland cells. Like nitroglycerol, it is an explosive, and its potassium and ammonium salts are extensively employed for this purpose. The substitution of three H atoms by the negative NO_2 groups in picric acid evidently increases its acidity, i.e., its dissociability into H^+ ions (cations)

and anions of the rest of the molecule (see exp. below).

Picric acid is now used medicinally, mainly as an antiseptic. In addition it seems to have an anæsthetic action on burns.

By the action of phenol-sulphonic acid on nitrates production of picric acid results. This is the basis of one of the methods of estimating small quantities of nitrates, as in water for drinking purposes.



EXPERIMENTS. (1) *Prepare picric acid.* Put 10 gm. of C.P. HNO_3 into a flask, add slowly 10 gm. of phenol. When the action has subsided add 30 gm. of fuming nitric acid and boil until the liquid becomes yellow. Cool, dilute the crystalline mass with water, and filter with suction. Wash the crystals with water, and recrystallize from a considerable quantity of hot water which has been acidulated with 5 drops of H_2SO_4 :



(2) Warm gently a little picric acid with 5 c.c. of petroleum ether in a test-tube; a colourless solution is secured (no ionization). Pour the petroleum ether into water and shake; the water becomes yellow from the picric acid dissolved in it (ionization).

(3) Immerse pieces of woolen, silk, and cotton cloth in picric acid solution for fifteen minutes. Wash them thoroughly with running water. Which are dyed?

Aminophenols (see p. 343).

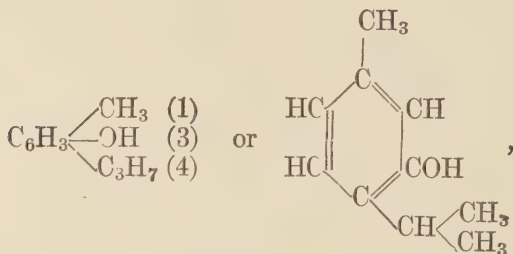
Phenolsulphonic acids (see p. 343).

Cresols (hydroxytoluenes), $C_6H_4 \begin{smallmatrix} \diagup CH_3 \\ \diagdown OH \end{smallmatrix}$. In accordance with the theory it is possible, by starting from the corresponding toluene-sulphonic acids or toluidiness to obtain three cresols, viz., ortho, meta, and para. Cresol (chiefly para) may be excreted in the urine in combination with sulphuric acid, exactly as in the case of phenol (p. 305). The cresols are contained, along with *guaiacol*, in **creosote**, a product of wood-tar, and sometimes used as an antiseptic. It is very difficult to separate the individual cresols from creosote. Cresol is also produced in the intestine by the action of microorganisms on protein. **Creosotal** is the carbonate of creosote. **Lysol** is a mixture of cresols with soap, and is said to be as strongly germicidal but less irritating than phenol. **Creolin** forms with water an emulsion of cresols. These substances possess antiseptic properties and are less poisonous than phenol. They are extensively used for disinfecting purposes.

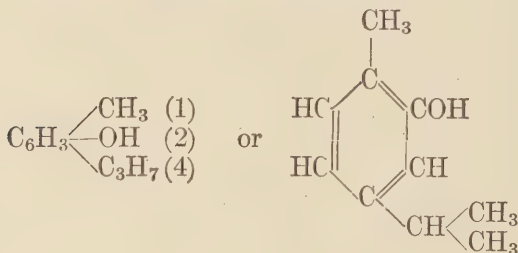
Parahydroxytolyl mustard oil, obtained by hydrolysis of **sinalbin** (p. 267), is a thiocyanate derivative of para cresol, $C_6H_4 \begin{smallmatrix} \diagup OH \\ \diagdown CH_2-CNS \end{smallmatrix}$.

Thymol and **carvacrol** are isopropyl cresols. That this is so is shown by the fact that they can both be converted into cymene, $C_6H_4 \begin{smallmatrix} \diagup CH_3 \\ \diagdown CH \end{smallmatrix} \begin{smallmatrix} \diagup CH_3 \\ \diagdown CH_3 \end{smallmatrix}$ (by removal of OH). They also give the reactions of phenols and

might therefore be considered as hydroxycymenes. Thymol is isopropylmetacresol,



and carvacrol is isopropylorthoeresol,



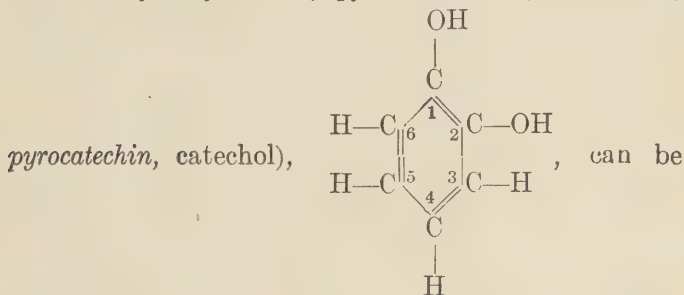
Thymol is contained in oil of thyme and is an antiseptic. It is crystalline and can be used for preserving urine. It is less poisonous than phenol. Melting-point 49.4° (corrected). Carvacrol is contained in *oil of caraway*.

Aristol is dithymol di-iodide. It is an antiseptic powder.

DIACID PHENOLS.

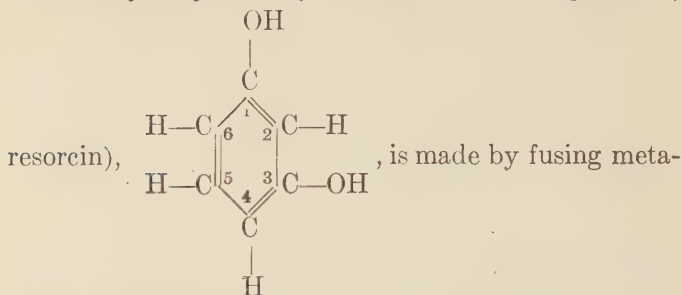
These are ortho, meta, and para. There is a gradation in melting-points, *o* 104°, *m* 119°, and *p* 169°. (Not all *o*, *m*, *p* compounds show consistent rise in melting-point in this manner.) They all have more or less marked reducing properties, and on this account some of them (especially hydroquinol) are used as developers in photography. With ferric chloride they all give colour reactions by becoming partially oxidized.

Orthodihydroxybenzene, pyrocatechol (1, 2-phen diol,



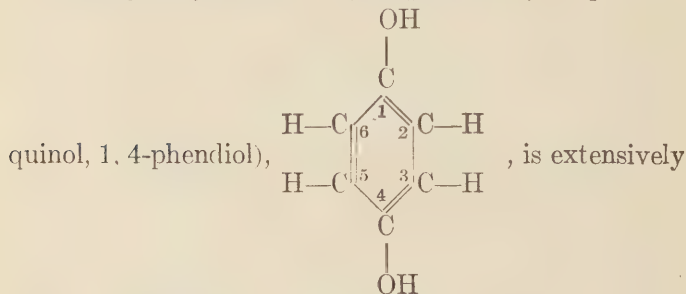
made by fusing orthophenol-sulphonic acid with caustic potash. It is soluble in water. By introducing a methyl radicle in place of a hydrogen atom of one hydroxyl group **guaiacol** (monomethyl ether of pyrocatechol, $C_6H_4 \begin{smallmatrix} \diagup OCH_3 \\ \diagdown OH \end{smallmatrix}$) is obtained. This latter can also be separated from beech-wood tar by distillation and crystallization, and is sometimes used, particularly as one of its compounds, in the treatment of phthisis. Guaiacol benzoate or **benzosol**, and guaiacol carbonate, or **duotal**, $(C_6H_4 \cdot OCH_3O)_2CO$, have also been much used as remedies for tuberculosis.

Metadihydroxybenzene, resorcinol (1, 3-phen diol,



benzene-disulphonic acid with caustic potash. Soluble in water, its solutions have a sweetish taste. When heated with phthalic acid it forms fluorescein (see exp., p. 325), and with sodium nitrite a blue pigment, *laccmoid*, solutions of which turn red with acids.

Paradihydroxybenzene, hydroquinol (hydroquinone



used in photography.

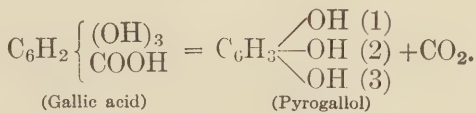
Dihydroxytoluene, orcinol (orcin), C_6H_3 $\begin{matrix} \nearrow CH_3 & 1 \\ \searrow OH & 3 \\ \nearrow OH & 5 \end{matrix}$, is

prepared by fusing 1, 3, 5-chlortoluene-sulphonic acid with caustic potash. By treatment with ammonia it absorbs oxygen from the air and is converted into *orcein*, $C_{28}H_{24}N_2O_7$, which dissolves in alkalis to form

a dark-red dye. Orcein is used in histology. It is contained in the natural dye archil, which is prepared, like litmus, by exposing powdered lichens suspended in ammoniacal solution to the action of the air.

TRIACID PHENOLS.

Pyrogallol (*pyrogalllic acid*, 1, 2, 3-phentriol) is 1, 2, 3 (*adjacent*, see p. 293) trihydroxbenzene, $C_6H_3(OH)_3$, and is prepared by the dry distillation of gallic acid (see exp below):



It forms fine needle-shaped crystals and is easily soluble in water. The solution when made alkaline greedily absorbs oxygen from the air, so that it is used for this purpose in gas analysis (see exp. below). Carbonates and acetates along with some carbon monoxide gas are produced by the oxidation. It is also extensively employed as a developer in photography.

Phloroglucinol (*phloroglucin*, 1, 3, 5-phentriol), $C_6H_3(OH)_3$, is 1, 3, 5 (*symmetrical*) trihydroxybenzene, and is obtained by the action of caustic potash on *phloretin*, which is split off from the glucoside phloridzin (see p. 267) by boiling the latter with acids.

Phloroglucinol is also employed along with vanillin in alcoholic solution as an indicator. (*Günzberg's reagent*) for free mineral acid. On evaporating a drop of this

reagent, mixed with the acid solution, to dryness it gives a deep-red stain if mineral acid is present.

Filicic acid, $C_{35}H_{38}O_{12}$, the most active constituent of aspidium, has a complex structural formula consisting of three rings linked together through intermediate C atoms, two of the rings being derivatives of phloroglucinol.

Hydroxyhydroquinol is asymmetrical tri-hydroxybenzene.

EXPERIMENTS. (1) Carefully heat 5 gm. of dry gallic acid in a retort or sublimation apparatus; carbon dioxide is evolved and pyrogallol sublimes. Test some of the latter with dilute ferric chloride solution; an intense blue-black colour is obtained.

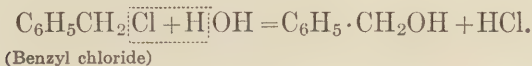
(2) Put 1 gm. of pyrogallol into a dropping funnel, add 10 c.c. of strong NaOH solution, cork tightly, and shake vigorously for a few minutes. Connect the stem of the funnel (after filling the stem with water) with a burette, the burette and tubing being full of water, open the cock, whereupon the water rises to take the place of the oxygen that has been absorbed.

Level up the water in the burette and the funnel, then read from the burette how much water was required to replace the oxygen that was absorbed. By finding how much more water is needed to completely fill the funnel, the volume of unabsorbed air (N_2) is easily determined.

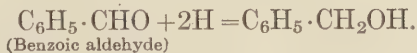
(3) Test solutions of resorcinol and pyrocatechol with ferric chloride; colour reactions are obtained.

AROMATIC ALCOHOLS (AND ALDEHYDES)

Besides the above, we may also have hydroxy derivatives of benzene where the hydroxyl group, instead of replacing one of the hydrogens of the benzene nucleus, is connected with a side chain. The best example is **benzyl alcohol**, $C_6H_5 \cdot CH_2OH$, which is *phenyl carbinol*. In their reactions such alcohols differ entirely from phenols and indeed possess all the properties of fatty primary alcohols. Thus, benzyl alcohol can be prepared by boiling benzyl chloride for some time (6-8 hours) with water (*cf.* synthesis of methyl alcohol, p. 113):



The Cl group, being in this case connected with a side chain and not with the benzene nucleus, is easily replaceable by OH. Benzyl alcohol may also be made by treating benzoic aldehyde (oil of bitter almonds) with nascent hydrogen:



The reactions of this alcohol agree with those of fatty alcohols: oxidation yields first an aldehyde (benzaldehyde) and then an acid (benzoic); ethers, such as benzyl methyl ether ($C_6H_5 \cdot CH_2O \cdot CH_3$), and ethereal salts, such as benzyl acetate ($C_6H_5CH_2 \cdot OOCCH_3$), are easily obtained. There are also substitution

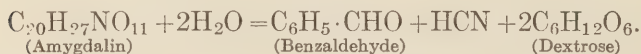
products (which, however, are not obtained by direct treatment) where one or more of the H atoms of the nucleus are replaced, e.g., chlorbenzyl alcohol, $\text{C}_6\text{H}_4\text{Cl}\cdot\text{CH}_2\text{OH}$.

Benzyl alcohol, however, differs in many respects from aliphatic alcohols: for instance, it does not form an ester with sulphuric acid. Its boiling-point is 206.5° .

The *homologues* of benzyl alcohol are of two kinds: (a) those in which the phenyl group remains unchanged, but the alcoholic side chain contains some higher fatty radicle, and (b) those in which the alcoholic side chain remains unchanged (i.e., remains as carbinol), but one or more of the H atoms of the benzene nucleus become replaced by radicles, as in tolyl carbinol, $\text{C}_6\text{H}_4\begin{matrix} \text{CH}_3 \\ \diagup \\ \text{CH}_2\text{OH} \end{matrix}$.

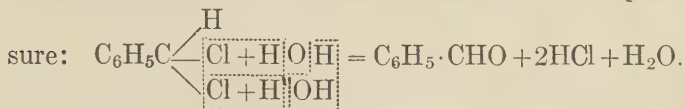
These alcohols, since they contain the primary alcohol group, can be oxidized to aldehydes and acids.

Benzoic aldehyde (benzaldehyde, oil of bitter almonds), $\text{C}_6\text{H}_5\cdot\text{CHO}$, is an important substance, being very reactive and therefore much employed for organic synthesis. Besides being produced by oxidation of benzyl alcohol, it can be obtained by the action of a hydrolyzing ferment—emulsin—on amygdalin, a glucoside contained in bitter almonds, the stone of the peach, etc. (see p. 266). The emulsin is usually present along with the amygdalin. Hydrocyanic acid is also produced during the reaction:



It can also be prepared by distilling a mixture of a

benzoate and a formate, and by heating benzal chloride, $C_6H_5CHCl_2$, with water and milk of lime under pressure:

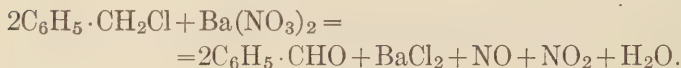


It is an oil of a pleasant odour, boiling at 179° and having a specific gravity of 1.0504 at 15° . Although relatively insoluble in water, it is used as a flavouring agent. It is not poisonous. Like other aldehydes, it forms addition products with such substances as hydrocyanic acid and acid sulphites. It also combines with alcohols, acids, ketones, etc., and forms a hydrazone (see p. 338) with phenylhydrazine, $C_6H_5 \cdot CH = N \cdot NH \cdot C_6H_5$. By boiling a solution of benzyl aldehyde in dilute alcohol containing some potassium cyanide, two molecules of it condense, forming *benzoin*, $C_6H_5 \cdot CHOH \cdot COC_6H_5$. In contact with air benzaldehyde readily oxidizes to benzoic acid, and with nascent hydrogen it combines to form benzyl alcohol. Like other aldehydes, it is a reducing agent; thus, it reduces ammoniacal $AgNO_3$, forming a mirror.

When benzaldehyde is treated with acetic anhydride, *benzoyl acetyl peroxide*, $C_6H_5 \cdot CO - O - O - OC \cdot CH_3$, is produced. The formula is comparable to that of hydrogen peroxide, $H - O - O - H$. This is called **acetozone** (or benzozone) and is believed to have strong germicidal powers by virtue of being a peroxide. It is used therapeutically for intestinal disorders.

Any aromatic aldehyde when shaken with strong KOH and allowed to stand undergoes oxidation and reduction simultaneously, the product being equal quantities of alcohol (reduction) and acid (oxidation).

EXPERIMENTS. (1) To 5 c.c. of benzyl chloride in a small flask add 50 c.c. of water and 5 gm. barium nitrate, and some capillary tubes (to prevent bumping). Attach to a reflux condenser and boil for two hours. If unchanged benzyl chloride is still present, filter, Cool, add a few c.c. of ether, draw off the bottom layer with a pipette. Shake with three portions of ether in a separating funnel. Evaporate the ether. Note the oily drops and the odour of benzaldehyde. Add some Schiff's reagent and warm; a beautiful colour is developed. The colour is intensified on heating, because benzaldehyde is soluble in hot water but only slightly soluble in cold water.



(2) To some solution of phenylhydrazine in dilute acetic acid add a few drops of benzaldehyde. Collect the precipitate and crystallize it from alcohol. The crystals of hydrazone melt at 152°.

(3) Spread a drop of benzaldehyde on a watch-glass, and let it stand until crystals of benzoic acid appear.

(4) Mix 10 c.c. of benzaldehyde and 12 c.c. of alcohol in a small flask. Add 10 c.c. of 10% KCN solution, now heat, using a reflux condenser, for thirty minutes. Cool, filter off the crystals of benzoin, and recrystallize from hot alcohol.

(5) To a solution of amygdalin add emulsin, cork the tube, keep at 40° some hours, note the odour, also test with Schiff's reagent.

CHAPTER XXVI.

AROMATIC ACIDS.

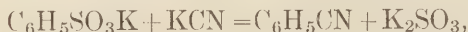
MONOBASIC ACIDS.

AROMATIC acids are in general analogous with those of the paraffins, being monobasic, dibasic, etc. The representative *monobasic* acid is **benzoic**, $\text{C}_6\text{H}_5\cdot\text{COOH}$. This acid is of great commercial value and of much physiological interest, since, as will be explained later, it is the end product of the oxidation in the animal body of a large number of benzene derivatives having oxidizable side chains.

It can be prepared by numerous reactions, the most important of which are as follows:

1. By oxidation of *any* benzene derivative with a single fatty side chain. It follows from this that if an aromatic substance yields benzoic acid on oxidation, it must contain only one side chain. When two side chains exist a dibasic acid (phthalic) is obtained. Thus the hydrocarbons of the benzene series, $\text{C}_6\text{H}_5\text{CH}_3$, $\text{C}_6\text{H}_5\text{C}_2\text{H}_5$, $\text{C}_6\text{H}_5\text{C}_3\text{H}_7$, their monacid alcohols and aldehydes, $\text{C}_6\text{H}_5\text{CH}_2\text{OH}$, $\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{OH}$, $\text{C}_6\text{H}_5\text{CHO}$, etc., and their halogen derivatives where the halogen is situated in the side chain, all yield benzoic acid when oxidized.

(2) By hydrolysis of benzonitrile, C_6H_5CN (see p.185). The reagent can be obtained by substituting the CN group for an H of benzene, either by distilling potassium benzene sulphonate with potassium cyanide,

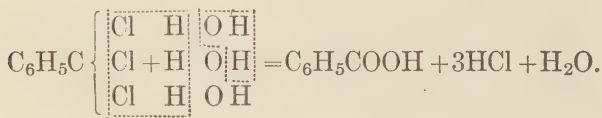


or by heating a diazonium salt with $Cu_2(CN)_2$ (see p. 335).

3. By treating *benzoyl chloride* (see p. 321) with water,

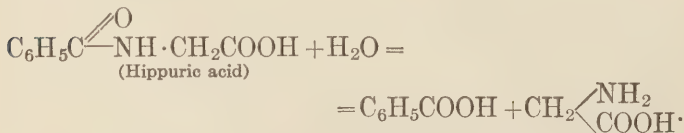


4. Commercially, benzoic acid is obtained by treating boiling toluene with chlorine, whereby *benzotrichloride*, $C_6H_5CCl_3$, is produced, which is then boiled with water (see exp. below):



5. From gum benzoin by sublimation or treatment with alkalis.

6. By heating hippuric acid (see p. 322) with hydrochloric acid (hydrolysis):



Benzoic acid forms needle-shaped crystals which melt at 121.3° (corrected) and readily sublime. Relatively insoluble in cold water, its solubility increases with rise

in temperature until, at 90° , the water contains 11.2% of the acid, and the crystals that remain undissolved liquefy and form a layer beneath the water. On further raising the temperature in a closed tube the two layers gradually mix till, at 116° , a homogeneous liquid is obtained. Salicylic acid (p. 346) behaves in a similar manner. The lower liquid layer is a solution of water in the acid, not melted acid. It is soluble in alcohol and ether, and volatilizes with steam. Its salts and derivatives are very numerous, and are analogous with those of acetic acid. Most of them are soluble in water.

Of the *metallic salts* those of sodium and ammonium are employed as medicines.

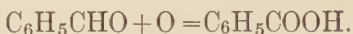
The *ethereal salts* are prepared in the same way as are those of acetic acid (see exp. (1). (a)).

Balsams (e.g., balsam of Tolu and balsam of Peru) contain as their important constituents benzoic and cinnamic acids, both as free acids and as their esters in combination with benzyl alcohol. *Gum benzoin* is a balsam containing benzoin.

EXPERIMENTS. (1) *Preparation of benzoic acid*. Put into a flask 5 c.c. of benzotrichloride, 100 c.c. of water, and small pieces of pumice. Attach to a reflux condenser and boil for two hours. Before cooling add 200 c.c. of hot water and filter at once. Cool, collect the crystals on a filter, recrystallize from hot water, and make the ethyl benzoate test on the dried crystals as follows: to some of the dried benzoic acid add 1 c.c. of alcohol and about 3 c.c. of concentrated H_2SO_4 . Heat; just as it begins to boil, notice the peppermint-

like odour of ethyl benzoate. Save a sample of benzoic acid.

(2) Heat together 1 c.c. of benzaldehyde and an excess of potassium permanganate solution until the odour of benzaldehyde is imperceptible. Add permanganate as required to maintain a pink colour. Decolorize with a few drops of alcohol. Cool, filter, and add HCl to the filtrate; benzoic acid crystallizes out:



(3) Sublime benzoic acid from impure benzoic acid, (see p. 12).

Benzoyl chloride, the acid chloride of benzoic acid, $\text{C}_6\text{H}_5\text{COCl}$, can be obtained by the action of chlorine on benzaldehyde, or by the action of PCl_5 on benzoic acid: $\text{C}_6\text{H}_5\text{COOH} + \text{PCl}_5 = \text{C}_6\text{H}_5\text{COCl} + \text{POCl}_3 + \text{HCl}$. It is more stable than acetyl chloride, not being decomposed by water in the cold. It resembles acetyl chloride, however, in that it reacts with the hydroxyl group of alcohols to form esters of benzoic acid. The presence of caustic alkali greatly facilitates this reaction. It reacts thus with the hydroxyl groups in dextrose, the resulting ester being insoluble in water and in dilute alkali.

EXPERIMENT. To 10 c.c. of 10% NaOH add 4 drops of glycerol and 1 c.c. of benzoyl chloride. Cork the tube, shake until a curdy precipitate forms, cooling the tube frequently. Add 10 c.c. of water, shake and filter. Crystallize the glyceryl tribenzoate from 15 c.c. of hot 65% alcohol.

The *substitution products* of benzoic acid are numerous, for of each there may be an ortho, meta, and para

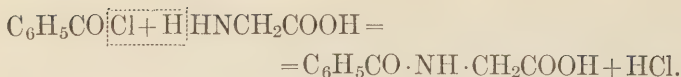
variety. They can be made by oxidizing the corresponding substituted toluenes, or by direct substitution of one or more of the hydrogens of the phenyl radicle in benzoic acid, by the same methods as are used for the substitution products of benzene. The chlorbenzoic acids, the nitrobenzoic acids, the aminobenzoic acids, and the sulphobenzoic acids are examples (see p. 355). The aminobenzoic acids are weaker than benzoic acid, while the nitrobenzoic acids are stronger.

Novocaine is a derivative of para-aminobenzoic acid, $C_6H_4(NH_2)COO-CH_2 \cdot CH_2-N(C_2H_5)_2 \cdot HCl$. It is built up from ethane by substitution of an H in each CH_3 group, diethylamine hydrochloride being the second substituting group. It is a local anæsthetic, introduced as a substitute for cocaine.

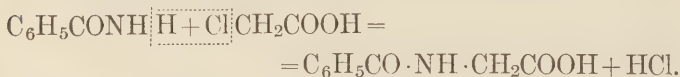
Stovaine and *alypin*, local anæsthetics of somewhat similar nature, are also benzoic acid derivatives.

An important compound of benzoic acid, from a biochemical standpoint, is **hippuric acid**. This is benzoyl-aminoacetic acid, $C_6H_5CO \cdot NH \cdot CH_2COOH$. It is present in the urine of herbivorous animals, being produced in the kidney by a synthesis of glycine and benzoic acid. It also appears in human urine when benzoic acid is administered, or when foods yielding it in the organism are ingested. It may be prepared in the laboratory by several methods:

1. Heating glycocholic acid and benzoic acid to 160° in a closed tube.
2. Shaking glycine dissolved in sodium hydroxide solution with benzoyl chloride (see exp. below):



3. Heating *benzamide* with chloroacetic acid (*benzamide* is analogous to *acetamide*, see p. 219):



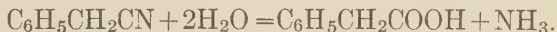
Hippuric acid is relatively insoluble in cold water, alcohol, and ether, and forms long rhombic crystals, having a melting-point of 187.5° (corrected). It is readily decomposed by boiling with acids or alkalis, and also decomposes when urine containing it undergoes fermentation.

EXPERIMENTS. (1) *Synthesize hippuric acid*. Shake together 4 c.c. of benzoyl chloride and a solution of 2.5 gm. of glycocoll in 30 c.c. of 10% NaOH until the odour of the chloride has disappeared. Cool whenever the mixture gets hot. Filter, acidulate the filtrate with HCl. Collect the hippuric acid on a filter, wash with little water, press dry between filter-paper, and recrystallize from hot water. Save a sample. Test part of it as follows (exp. 2).

(2) (a) Test the solubility of hippuric acid in petroleum ether (compare benzoic acid). (b) Heat a little dry hippuric acid in a test-tube; benzoic acid sublimes, while the residue becomes reddish.

Corresponding to *toluene* there are four monobasic **toluic acids**. Three of these (*o*-, *m*-, *p*-) have the formula $\text{C}_6\text{H}_4 \begin{smallmatrix} \text{CH}_3 \\ \diagup \\ \text{COOH} \end{smallmatrix}$ and are made by oxidizing the

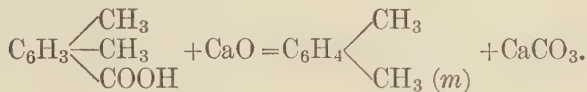
corresponding xylenes with nitric acid. The fourth has the formula $C_6H_5CH_2COOH$ and might properly be called **phenyl-acetic acid**. It is obtained by treating benzyl chloride, $C_6H_5CH_2Cl$, with potassium cyanide and hydrolyzing the resulting nitrile ($C_6H_5CH_2CN$):



A homologue of this is phenyl-propionic or **hydro-cinnamic acid**, $C_6H_5CH_2CH_2COOH$.

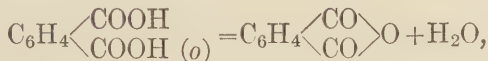
Mandelic acid is a hydroxy acid, its formula being $C_6H_5 \cdot CHOH \cdot COOH$.

Mesitylene yields only one acid, **mesitylenic**, $C_6H_3 \begin{matrix} \swarrow CH_3 \\ \text{---} CH_3 \\ \searrow COOH \end{matrix}$. This is of importance because it can be converted into metaxylene by distillation with lime (cf. benzene, p. 285):



DIBASIC ACIDS.

In agreement with theory, there are three of these. They are called **phthalic acids**. Orthophthalic acid is prepared by oxidizing naphthalene (see p. 368) with sulphuric acid, or by oxidizing *o*-toluic acid with potassium permanganate. When heated it decomposes into water and an anhydride,

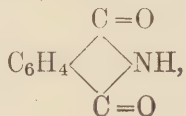


which latter, when heated with phenols in the presence of H_2SO_4 , yields phenolphthalein (see exp. 3), a body of

complicated structure used extensively as an indicator in volumetric analysis, being red in alkaline and colourless in acid solution (see p. 358). It is also used now as a cathartic.

The meta- and paraphthalic acids do not form anhydrides. Certain iodine derivatives of phenolphthalein, as *nosophen*, *eudoxine*, and *antinosine*, are used as medicines.

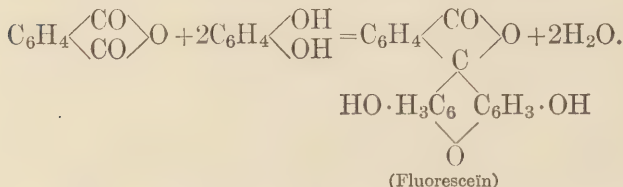
When phthalic anhydride is acted upon by ammonia an acid imide, *phthalimide*,



is formed.

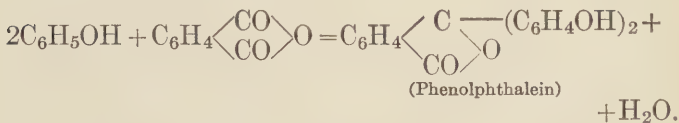
EXPERIMENTS. (1) Heat some phthalic acid in a sublimation apparatus (see p. 12); the sublimate is phthalic anhydride.

(2) To some phthalic anhydride add an equal quantity of resorcinol and 1 c.c. of concentrated H_2SO_4 , then warm until deep red. Dilute with 100 c.c. of water and render alkaline with NaOH . The resulting solution of *fluoresceïn* is pinkish to transmitted light, but shows a marked greenish fluorescence to reflected light:



(3) Mix equal quantities of phthalic anhydride and phenol, add a little C.P. H_2SO_4 , and warm until strongly

coloured. Pour into a large quantity of water. This solution of phenolphthalein becomes red when it is made faintly alkaline:



(4) Prepare **eosin**. Dissolve 2 gm. of fluoresceïn in 7 c.c. of glacial acetic acid, add to it 0.5 c.c. bromine dissolved in 6 c.c. acetic acid. Mix and warm until dissolved. Then add water; red crystals of eosin separate out. To a little of the eosin add NaOH solution, the eosin now dissolves, forming a solution of characteristic red colour.

There is a *hexabasic* acid, viz., **mellitic**, $\text{C}_6(\text{COOH})_6$, which is found in nature in combination with aluminium as the mineral mellite.

CHAPTER XXVII.

AROMATIC NITROGEN AND SULPHUR DERIVATIVES.

THERE is very little similarity between the nitrogen compounds of the aromatic bodies and those of the paraffins. The nitro compounds of the paraffins we have seen to be of little importance; those of the aromatic bodies, on the other hand, are of prime importance, because they are readily produced and are easily converted into other nitrogenous derivatives. On this account *nitration* forms the first step in many organic syntheses.

NITRO COMPOUNDS.

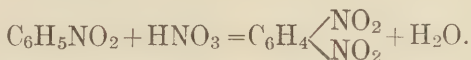
By shaking benzene in the cold with a mixture of pure nitric and sulphuric acids, **mononitrobenzene**, an oily liquid is obtained.¹ The sulphuric acid absorbs the water produced: $C_6H_6 + HNO_3 = C_6H_5NO_2 + H_2O$. Its boiling-point is 210° , melting-point 5° and its specific gravity 1.2033 at $\frac{20^\circ}{4^\circ}$.

EXPERIMENT. To 80 c.c. H_2SO_4 in a flask add, while shaking, 70 c.c. of colourless HNO_3 . Cool thoroughly. Add (a little at a time) 20 c.c. of benzene, keeping the temperature of the mixture below 30° and shaking frequently. Take 30 minutes for the work of

¹ Mononitrobenzene has the odour of bitter almonds and is known as essence of mirbane. It is poisonous.

adding the benzene. Attach a vertical air-condenser tube; heat for an hour in a bath kept at 60°, shaking occasionally. Cool, dilute with 120 c.c. of water, pour into a separating funnel, draw off the bottom layer of acid, and wash the oil with water (the nitrobenzene becomes the bottom layer). Warm gently with dry calcium chloride in a flask on a water-bath. Distil in a fractionating flask, when the temperature rises above 100° attach an air-condenser, and observe the boiling-point. Note the odour of the distillate.

If, on the other hand, the reaction be allowed to proceed at boiling temperature and with fuming nitric acid the product is **dinitrobenzene**, a crystalline substance (needles) melting at 90° (corrected) and boiling at 297°:



Three varieties of this are possible (see p. 291).

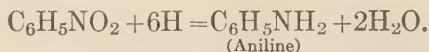
EXPERIMENT. *Prepare dinitrobenzene (meta).* Mix in a beaker 25 c.c. of C.P. H_2SO_4 and 25 c.c. of fuming HNO_3 . Immediately add very slowly 5 c.c. of benzene from a pipette. After the action subsides, boil for a while and then pour the mixture into 250 c.c. of cold water. Filter off the precipitate, press between filter-paper, and crystallize from alcohol. Make a melting-point determination with dried crystals. Save a sample of the crystals.

Toluene and the xylenes react with nitric acid in the same manner. In fact, the more alkyl groups there are attached to the benzene nucleus, the more easily can

nitro groups be introduced into it. The nitro compounds are very stable.

AMINO COMPOUNDS.

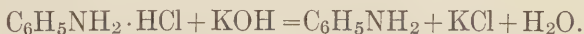
The most important reaction of nitro compounds is with nascent hydrogen, whereby they become converted into amino compounds, of which **aniline** (phenylamine) is the representative:



Commercially, aniline is produced by mixing nitrobenzene with iron filings and hydrochloric acid in an iron cylinder provided with a stirring apparatus, and, when the action is over, adding lime and distilling the aniline. It is a colourless liquid, boiling at 183.7° (corrected); its specific gravity at 16° is 1.024. If not perfectly pure it becomes coloured on standing. It is soluble in about 30 parts of water, and one part of water is soluble in about 20 parts of aniline at 25° . It is readily soluble in alcohol. It gives several important colour reactions, described in the experiments below. It may be considered as NH_3 in which one H is displaced by C_6H_5 . Like all such bodies (see p. 187), it directly combines with acids to form (aniline) salts, e.g., $\text{C}_6\text{H}_5\text{NH}_2 \cdot \text{HCl}$; $\text{C}_6\text{H}_5\text{NH}_2 \cdot \text{HNO}_3$; $\text{C}_6\text{H}_5\text{NH}_2 \cdot \text{H}_2\text{SO}_4$. The hydrochloride is technically known as *aniline salt*. In watery solution, however, aniline is not alkaline towards litmus and scarcely conducts an electrical current; in other words, it does not become ionized (see p. 57). It is, therefore, quite different in this respect from aliphatic amines, which with water form bases, some of which

are stronger even than ammonia (*cf.* p. 189). Phenyl (C_6H_5) diminishes the basic properties of the amino (NH_2) group, whereas fatty residues increase the basic properties of NH_2 . Whereas nitrous acid decomposes fatty amines with liberation of nitrogen (p. 189), it converts aromatic amines into diazonium compounds (p. 334).

Aniline can be liberated from the acid in its salts by distilling with caustic alkali:



It can also be obtained by distilling indigo (hence its name, *anil* being the Spanish for indigo). It is an extremely important substance in organic synthesis.

EXPERIMENTS. (1) *Preparation of aniline.* Put 30 gm. of granulated tin and 15 c.c. of nitrobenzene into a large flask, add gradually (in portions of 5 c.c. each) 100 c.c. of C.P. HCl, and cool the flask whenever the action becomes very vigorous. When all the acid has been added, heat on a water bath for one hour, using a vertical air-condenser. Now dilute with 50 c.c. of water, cool to room temperature, pour into a separating funnel and shake with ether to remove unchanged nitrobenzene. Add 50% NaOH until strongly alkaline; cool the flask if the mixture boils. Distil with steam. When the distillate comes clear, stop the process. Add to the distillate 25 gm. NaCl for each 100 c.c.; shake in a separating funnel with three portions of ether. Dry the ether extract with solid potassium hydroxide. Next empty the liquid into a fractionating flask, distil off the ether, then distil the aniline, using an air-condenser.

(2) *Tests* (a) Dissolve a little KClO_3 in 0.5 c.c. H_2SO_4 ; add a few drops of aniline solution—a blue-violet colour appears; dilute with water—the colour changes to red; then add ammonia, and the blue is restored. (b) To a solution of aniline in H_2SO_4 add a few drops of potassium dichromate solution—a blue colour appears. (c) To some aniline solution (in water) add a filtered solution of bleaching-powder—a purple colour develops.

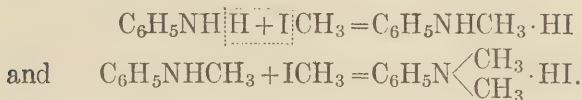
Derivatives of Aniline. The *homologues* include three **toluidines**, $\text{C}_6\text{H}_4\begin{smallmatrix} \diagup \text{CH}_3 \\ \diagdown \text{NH}_2 \end{smallmatrix}$, of which the ortho and para varieties are important, and six **xylydines**, $\text{C}_6\text{H}_3\begin{smallmatrix} \diagup (\text{CH}_3)_2 \\ \diagdown \text{NH}_2 \end{smallmatrix}$, this large number of isomers being due to differences in the relative positions of the amido and methyl groups. When a mixture of aniline and the toluidines is treated with oxidizing agents a compound known as **rosaniline** is obtained. This is the mother substance of the aniline dyes. Rosaniline is $(\text{NH}_2\text{C}_6\text{H}_4)_2\text{C}(\text{OH})\text{C}_6\text{H}_3\begin{smallmatrix} \diagup \text{CH}_3 \\ \diagdown \text{NH}_2 \end{smallmatrix}$. *Fuchsin* is rosaniline hydrochloride.

EXPERIMENT. Heat together in a test-tube 1 c.c. of aniline, 1 gm. of paratoluidine, and 3 gm. HgCl_2 until dark red in colour (15 minutes at $180\text{--}200^\circ$). Cool partly, extract with alcohol; a deep-red solution is obtained. Filter, evaporate the filtrate.

Replacement of one or more of the H atoms of the NH_2 group in aniline can be effected in various ways.

By reaction with alkyl halides secondary and tertiary

mixed aromatic fatty amines are obtained. Thus with methyl iodide, methyl aniline and dimethyl aniline are produced:



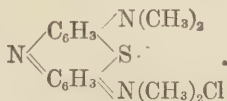
Some quaternary base is also formed by the reaction.

Dimethyl aniline is commercially the most important of these mixed amines and is prepared by heating aniline hydrochloride with methyl alcohol, methyl chloride being first formed, which then reacts as above.

Dimethyl aniline + chloranil ($\text{C}_6\text{Cl}_4\text{O}_2$) gives **methyl violet**, which is a mixture of two salts with the following formulæ:



Methyl violet is also called *pyoktanin*. Methylene blue (methylthionin hydrochloride) has the formula



In a similar manner replacement with phenyl groups may occur, di- and triphenylamine being produced.

Diphenylamine, $\text{C}_6\text{H}_5\text{NHC}_6\text{H}_5$, is obtained by heating aniline with aniline hydrochloride to 200° :

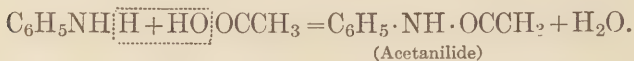


Dissolved in concentrated sulphuric acid it is a reagent which detects traces of nitric acid by formation of a deep blue colour. It is changed to tetra-phenylhydrazine.

With acid chlorides, aniline forms *anilides*, which are analogous with the acid amides (see p. 218):



One of these, **acetanilide** (phenylacetamide), is of very great therapeutic interest on account of its antipyretic properties. It is the active drug in many proprietary headache medicines (antikamnia, antifebrine, orange powders, etc.). These remedies are not entirely harmless, since acetanilide acts as a circulatory depressant. Acetanilide is easily prepared by heating aniline with glacial acetic acid (see exp.):



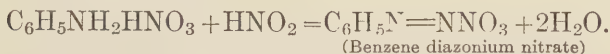
EXPERIMENT. Mix 10 c.c. each of aniline and glacial acetic acid in a small flask; fit with a long glass tube as a reflux condenser (allows some of the water of reaction to escape, but condenses the acetic acid); boil for four hours. Dilute with 100 c.c. of boiling water and filter at once, using a hot funnel. On cooling, acetanilide crystallizes out. Recrystallize from hot water. Save a sample.

Acetanilide is very slightly soluble in cold water and crystallizes from hot water in colourless plates. It

melts at 114.2° (corrected). Two other antipyretic drugs are closely related to acetanilide. In one of these, **exalgin** (methyl acetanilide), the hydrogen atom of the amido group is replaced by methyl, $\text{C}_6\text{H}_5\text{NCH}_3\text{COCH}_3$. In the other, **benzanilide** (benzoyl anilide), the acetyl radicle is replaced by benzoyl, $\text{C}_6\text{H}_5\cdot\text{NH}\cdot\text{OCC}_6\text{H}_5$.¹

DIAZO COMPOUNDS.

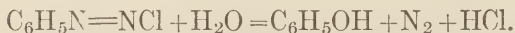
When fatty amino derivatives are treated with nitrous acid, (see p. 189), nitrogen is evolved and a hydroxyl group takes the place of the amino group; with the aromatic amines, on the other hand, nitrous acid at low temperatures has quite a different action. It converts them into **diazo compounds**, so called because they contain two nitrogen (nitrogen = *azote* (French)) atoms linked together. The diazo compounds are of very great importance in organic synthesis on account of the readiness with which they can be converted into other bodies. They are prepared by treating an ice-cold solution of an aniline salt with nitrous acid or with ethyl nitrite:



¹ In their passage through the animal body these drugs become partially oxidized to aminophenol $\text{C}_6\text{H}_4\begin{smallmatrix} \text{OH} \\ \diagdown \\ \text{NH}_2 \end{smallmatrix}$, which also has antipyretic properties, and it has been thought that it is really this substance which produces the antipyretic action. On this supposition, various derivatives of par-aminophenol have been prepared and found to be equally active as antipyretics. These will be described later on (p. 344). Acetyl paraminophenol as well as aminophenol is produced in the animal body.

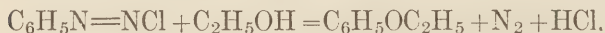
If a diazonium salt be dried and struck with a hammer it explodes. Its most important reactions are as follows:

1. *With water* it forms phenol and nitrogen (see exp. (2) (b)):

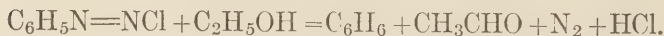


To obtain this result the diazonium salt is best prepared by treating a cold, acidified solution of an aniline salt with an equivalent quantity of sodium nitrite, and then boiling (see exp. 2, p. 303).

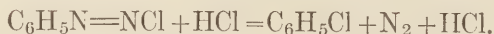
2. Boiling *with alcohol* causes replacement of the diazo group either by ethoxy ($-\text{O}-\text{C}_2\text{H}_5$) or hydrogen. In the first case phenyl ethyl ether or *phenetole* is formed:



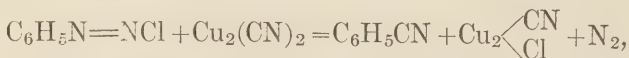
In the second case benzene and aldehyde:



3. Heating *with a halogen acid* or, better still, with an acid solution of the corresponding cuprous salt of the acid causes replacement of the diazo group by the halogen:



4. Heating *with cuprous cyanide* replaces the diazo group by cyanogen:



and the resulting nitrile can be hydrolyzed to form benzoic acid (see p. 319).

Other replacements by hydrocarbon residues, sulphur groups, etc., can also be effected.

EXPERIMENTS. (1) Prepare benzene diazonium nitrate. Put 50 gm. of arsenic trioxide into a flask; provide a funnel-tube, as in other gas-generators, and a delivery-tube which is connected with an empty bottle or cylinder standing in cold water. Mix 10 gm. of aniline nitrate with 12 c.c. of cold water in a graduate or large test-tube standing in ice-water, and immerse in the liquid a delivery-tube coming from the condenser-bottle of the gas apparatus. Through the funnel add 50 c.c. of concentrated HNO_3 to the As_2O_3 ; heat as is necessary to keep up an evolution of nitrogen oxides. Bubble the gas into the aniline nitrate mixture until complete solution is secured. Add to the solution an equal volume of alcohol cooled to 0° , then some cold ether. An abundant precipitate of benzene diazonium nitrate is obtained.¹ Filter quickly with suction. Test for the following reactions at once:

(2) (a) Dissolve some in water and let it stand. It decomposes, as is shown by change of colour. (b) Boil some with water; notice the phenol odour. (c) Boil some with alcohol in a test-tube; it is decomposed with production of phenetole. (d) Add some to a little con-

¹ A less troublesome method of preparation is as follows: dissolve 5 gm. aniline hydrochloride in 35 c.c. absolute alcohol which contains a few drops of concentrated HCl . Cool to 5° add 4 c.c. ethyl nitrite very slowly while shaking and cooling. Test for HNO_2 with starch iodide paper. Add more ethyl nitrite if necessary. Let it stand a while, then add cold ether.

centrated HCl and boil. Chlorbenzene is formed; on adding water this sinks to the bottom. (e) The dried salt is explosive; place a small particle on a piece of iron and strike it with a hammer.

In all the above cases the N_2 group is replaced. Diazo compounds, however, exhibit another type of reaction in which the N_2 group is retained and a new substance of greater stability is produced. The more important of these substances are:

a. Diazoamino Compounds. In these, one of the hydrogens of an amido group is replaced by a diazo residue. A type of the class is *diazoaminobenzene*, $C_6H_5 \cdot N=N \cdot NH \cdot C_6H_5$, which is prepared by bringing together aniline and diazonium chloride in neutral solution. It forms yellowish crystals, which are insoluble in water but soluble in alcohol. By heating with aniline, and in various other ways, diazoaminobenzene becomes converted by a rearrangement of atoms into

b. Aminoazobenzene, $C_6H_5 \cdot N=N \cdot C_6H_4 \cdot NH_2$, which is the amino derivative of a substance called azobenzene.

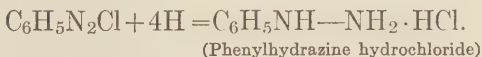
Dimethyl aminoazobenzene is $C_6H_5 \cdot N_2 \cdot C_6H_4 \cdot N(CH_3)_2$. It is used as an indicator for free acid, giving a pink colour in the presence of the latter (see p. 361).

c. Azobenzene, $C_6H_5 \cdot N=N \cdot C_6H_5$. Azobenzene can be obtained by partial reduction of nitrobenzene. It forms orange-red crystals and is soluble in water, but the resulting solution is not a dye (see p. 365). The azo group is present, however, in many dyes. It has been calculated that the number of azo dyes that can theoretically be prepared runs up into the millions.

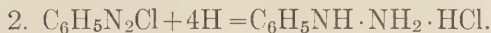
d. Hydrazobenzene, $C_6H_5NH-NHC_6H_5$, is obtained

by reducing azobenzene; it is colourless. Hydrazobenzene is the diphenyl derivative of *hydrazine*, $\text{NH}_2\text{—NH}_2$. The most important hydrazine derivative is

e. Phenylhydrazine, $\text{C}_6\text{H}_5\text{NH—NH}_2$, which forms hydrazones (see p. 316) with aldehydes, and osazones with sugars (see p. 250). It is obtained by reduction of diazonium salts (see exp.):

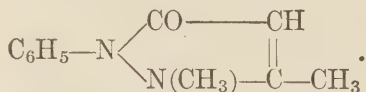


EXPERIMENT. To 18 c.c. of freshly distilled aniline add, while stirring, 100 c.c. of concentrated HCl. Cool, in a freezing mixture to 0° , add 150 gm. of ice, then add slowly, from a dropping funnel (have the tip dipping in the mixture), while shaking, a solution of sodium nitrite (14 gm. in 70 c.c. of water), until testing with starch-potassium-iodide paper shows the presence of free nitrous acid (blue colour). For the test dilute a drop of the acid mixture with 5 c.c. of water. During the diazotizing the temperature must keep below 5° . Add slowly an ice-cold solution of 60 gm. of stannous chloride in 50 c.c. of concentrated HCl. Add ice to keep the temperature at 0° . Mix thoroughly and let it stand one hour. Filter through muslin, using suction. Transfer to a porous plate, press out the phenylhydrazine hydrochloride crystals in a thin layer, and set away to dry out:



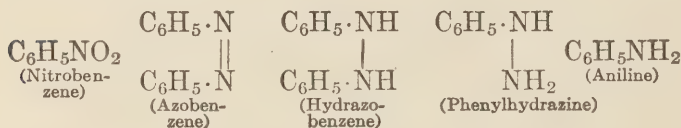
Free phenylhydrazine may be extracted by treating the hydrochloride with an excess of NaOH solution and shaking with ether. After dehydrating the ethereal extract, evaporate the ether; phenylhydrazine remains behind as a liquid which readily solidifies on cooling.

Phenylhydrazine is a colourless oil at ordinary temperature and boils at 242° , meanwhile undergoing some decomposition. It melts at 19° . It is poisonous. It becomes dark on exposure to air. Its salts, e.g., the hydrochloride, are solid and are sometimes employed in place of the base itself for producing osazone crystals, the hydrochloric acid being neutralized by sodium acetate. By a series of reactions, which are too complicated for description here, a derivative of phenylhydrazine can be obtained which lowers fever temperature. This is **antipyrin** or **phenazone** (1-phenyl-2,3-dimethyl pyrazolone),



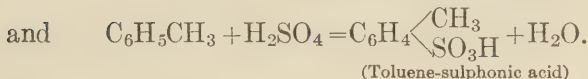
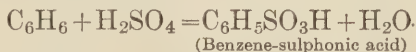
It is really a heterocyclic compound (p. 373). It acts as a weak base, certain of its salts being used medicinally, e.g., *tussol*, which is antipyrin mandelate.

The relationship of these bodies to nitrobenzene and aniline will be evident from an examination of the following formulæ:



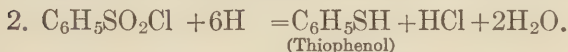
SULPHUR DERIVATIVES.

Sulphonic acids. With sulphuric acid the benzenes form sulphonic acids, thus:



It is of importance to note that in this respect they behave quite differently from paraffins. When an alkyl group (as in toluene), an amino group (as in aniline), or a hydroxyl group (as in phenol) is attached to the benzene nucleus, the sulphonic acid derivative is more easily formed than when benzene alone, or any of its other derivatives, is used.

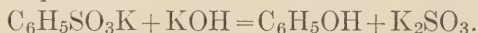
The sulphonic acids are soluble in water and are strong acids, so that their salts are very stable, e.g., $\text{C}_6\text{H}_5\text{SO}_3\text{Na}$. Treated with phosphorus pentachloride the salts of sulphonic acids form sulphonic chlorides, which may be reduced to mercaptans:



These reactions show us that sulphonic acids must possess an —OH group and that the S atom is in immediate connection with the benzene ring. The structural formula of benzene-sulphonic acid must therefore be $\text{C}_6\text{H}_5 \begin{array}{c} \diagdown \\ \text{HO} \end{array} \text{SO}_2$, or sulphuric acid, $\begin{array}{c} \text{HO} \\ \diagup \end{array} \text{SO}_2$, in which one hydroxyl group is replaced by phenyl (*cf.* p. 194).

They give several other reactions, the following of which are important:

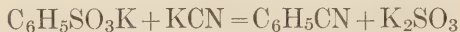
1. *Fused with potassium hydroxide*, benzene-sulphonic acid yields phenol,



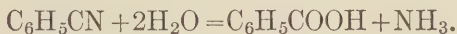
EXPERIMENTS. (1) To 75 gm. of fuming H_2SO_4 in a small flask to which an air-condenser is attached, add, a little at a time, 20 gm. of benzene, shaking and cooling after each addition. Transfer to a dropping funnel, and run the mixture out, drop by drop, into 300 c.c. of cold saturated NaCl solution. Keep the salt solution cold with ice-water. On standing, crystals of sodium benzene sulphonate form. Crystallization may be hastened by strongly cooling some of the mixture in a test-tube and emptying the crystalline mass into the main liquid. Filter the pasty mass of crystals with suction and wash it with a little saturated salt solution. Press dry, and complete the drying in an oven at 110° .

(2) Weigh the dry powder (of 1); weigh out five times as much KOH . Put the KOH in an iron dish, add a few cubic centimetres of water, and melt. Then add slowly, while stirring with a spatula, the sodium benzene sulphonate. Keep fused for an hour. Dissolve in water, acidulate with HCl , shake with ether, and treat the ethereal solution of phenol in the same way as in the previous phenol experiments (see p. 303).

2. *Distilled with potassium cyanide*, cyanides are formed:



By hydrolysis these cyanides can be converted into acids:



The toluene-sulphonic acids may be ortho or para. The meta variety is rare. The sulphonic acid group is present in many dyestuffs (see p. 366).

CHAPTER XXVIII.

MIXED AROMATIC COMPOUNDS.

HYDROXY COMPOUNDS.

INCLUDED under this head, we will consider certain compounds in which two or more dissimilar groups are attached to the benzene ring. It is evident that compounds of this nature must be extremely numerous. It will, of course, be possible here merely to indicate in a general way the more important of these. Besides the derivatives of the homologues of benzene which have already been described, the following are the most important mixed compounds:

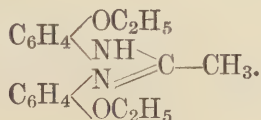
1. **Phenol and sulphonic groups** exist in phenol-sulphonic acid, $\text{C}_6\text{H}_4\begin{smallmatrix} \text{SO}_3\text{H} \\ \text{OH} \end{smallmatrix}$ (*o* or *p*), which is commercially known as *aseptol* and used as a disinfectant. The sodium salt of it is *sodium sulphocarbolate*, and is used to arrest fermentation in the stomach.

2. **Phenol and nitro groups** exist in mono- and trinitrophenol (picric acid), which have already been described (p. 306).

3. **Phenol and amino groups** exist in the aminophenols, which are prepared by reducing the mononitrophenols. The *para* variety is of therapeutic inter-

est. Its ethyl ether is known as *paraphenetidin*, $\text{C}_6\text{H}_4 \begin{smallmatrix} \diagup \text{OC}_2\text{H}_5 \\ \diagdown \text{NH}_2 \end{smallmatrix}$, and if this is treated with glacial acetic acid, acetaminophenetole is formed, $\text{C}_6\text{H}_4 \begin{smallmatrix} \diagup \text{OC}_2\text{H}_5 \\ \diagdown \text{NH} \cdot \text{OCCH}_3 \end{smallmatrix}$, which is known in medicine as **phenacetin** (or acetphenetidin) and is perhaps the safest antipyretic. Phenacetin is a white crystalline substance, sparingly soluble in water and with a melting-point of 135° .

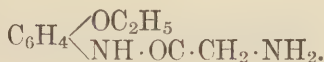
A number of other phenetidin derivatives are used in medicine, particularly holocain, lactophenin, and phenocoll. **Holocain** is



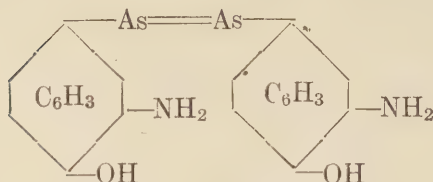
Lactophenin is lactylphenetidin,



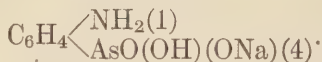
Phenocoll is aminoacetphenetidin,



An arsenic containing derivative of ortho amino-phenol has been recently synthesized. It is used as a remedy for syphilis. Its trade name, *arseno-benzol* (or "606"), does not give a correct idea of its composition. It is diamino-dihydroxy-diarseno-(di-) benzene,



Another organic arsenic compound is *atoxyl*, in which an OH of monosodium arsenate is replaced by aniline,



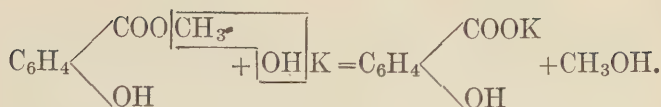
If the sodium be substituted by H , *arsanilic acid* is obtained. *Arsacetin* is sodium acetyl arsanilate.

4. **Phenol and a primary alcohol group** are combined in saligenin, $C_6H_4 \begin{matrix} \swarrow OH \\ \searrow CH_2OH \end{matrix}$. This exists in combination with dextrose in the glucoside **salicin** (see p. 267).

5. **An acid group** may exist along **with one or more hydroxyl group**. According to the number of the latter groups we may have mono-, di-, and trihydroxybenzoic acids.

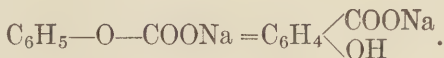
A. *Monohydroxybenzoic acids*, $C_6H_4 \begin{matrix} \swarrow OH \\ \searrow COOH \end{matrix}$. The *ortho* variety of this is **salicylic acid**, an extremely important medicinal substance. Oxidation of the alcohol saligenin (above) yields salicylic acid. It may be prepared by a variety of reactions, the chief of which are as follows:

(1) By saponifying methyl salicylate (oil of winter-green) with caustic potash.



The potassium salicylate thus formed can be decomposed by acidifying with hydrochloric acid (see exp. 1, below).

(2) By subjecting sodium phenolate to the action of carbon dioxide, sodium phenyl carbonate, $\text{C}_6\text{H}_5\text{OCOONa}$, is formed, which, by heating to 130°C . in an autoclave, becomes converted into sodium salicylate (an intramolecular change taking place):
salicylate:



This method is used commercially.

(3) By fusing orthotoluene-sulphonic acid, orthocresol, or orthosulphobenzoic acid with caustic potash. In the case of the first two bodies oxidation of the methyl side chain occurs. The replacement of the sulphonic group by hydroxyl has already been explained (*cf.* p. 302).

(4) By converting orthoaminobenzoic acid into the diazonium salt and boiling this with water (see p. 334).

Salicylic acid crystallizes in needles and melts at 159° (corrected). It is readily soluble in hot water, but only sparingly so in cold. Its aqueous solutions give an intense violet colour with ferric chloride. It is readily soluble in fat-solvents. Solutions of salicylic acid possess antiseptic properties, and, having no odour, it is therefore employed for preserving wines, foods, etc.

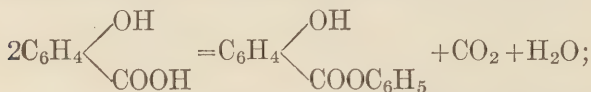
Its sodium salt, $\text{C}_6\text{H}_4\begin{smallmatrix} \diagup \text{COONa} \\ \diagdown \text{OH} \end{smallmatrix}$, has great medicinal value in the treatment of rheumatism.

There are also *meta* and *para* hydroxybenzoic acids, which can be prepared from the corresponding amino- or sulphonic-benzoic acids. They do not react with ferric chloride.

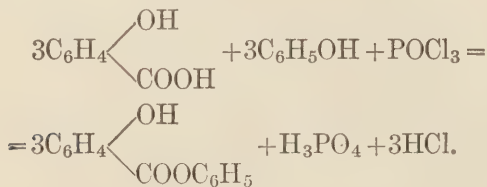
The *meta* and *para* acids are weaker acids than salicylic acid, and have a somewhat different physiological action. The introduction of OH in the ortho position increases the acid power of the molecule, so that salicylic acid is much stronger than benzoic acid.

Salicylic acid forms various salts, the salicylates, many of which are important. **Methyl salicylate**,

$\text{C}_6\text{H}_4\begin{smallmatrix} \diagup \text{OH} \\ \diagdown \text{COOCH}_3 \end{smallmatrix}$, is the chief constituent of oil of wintergreen. It can be made synthetically by heating methyl alcohol with sulphuric acid and salicylic acid. A very interesting compound of salicylic acid is phenyl salicylate, $\text{C}_6\text{H}_4\begin{smallmatrix} \diagup \text{OH} \\ \diagdown \text{COOC}_6\text{H}_5 \end{smallmatrix}$, or **salol**. It is produced by heating salicylic acid alone to $200^\circ\text{--}220^\circ$ (see exp.).



or by heating phenol and salicylic acid in the presence of phosphorus oxychloride:



Salol is a white crystalline powder, somewhat aromatic in odour and melting at 43° . It is insoluble in water and unaffected by dilute acids. Alkalies readily saponify it, however, and yield salicylate and phenol. Taken internally it will therefore remain undecomposed till it reaches the intestine, when the phenol and salicylate liberated by action of the alkali will act as antiseptics. On this account it is used for intestinal antiseptics.

By the action of sulphuric acid on salicylic acid, **salicyl-sulphonic acid**, $C_6H_4 \begin{matrix} \text{COOH(1)} \\ \text{OSO}_3\text{H(2)} \end{matrix}$, is formed. This is a white crystalline deliquescent substance, readily soluble in water, the solution being a valuable precipitant for certain but not all proteids. Its solutions on standing become coloured red.

EXPERIMENTS. *Salicylic acid*. (1) Saponify 5 c.c. of oil of wintergreen by boiling with 100 c.c. of 20% NaOH, using a reflux condenser, until the oil has disappeared. Cool, acidulate with HCl, collect the crystals on a filter, and wash them with a small quantity of water. Dissolve the salicylic acid in a little hot alcohol, and filter the solution into a beaker half full of cold water. Collect the crystals.

(2) Tests. (a) Add ferric chloride solution to some salicylic acid solution—violet-blue colour. Compare the similar phenol test. Try ferric chloride with alcoholic solutions of phenol and of salicylic acid. (b) Mix a little salicylic acid with some soda-lime and heat in a dry test-tube until the odour of phenol is noticed.

(3) *Prepare salol* as follows: Fill a dry test-tube

one third full of salicylic acid, fit the test-tube with a cork having a piece of small glass tubing 8 inches long passing through it, now heat gradually, boil the melted salicylic acid for five minutes, and, removing the cork, pour the hot liquid into some cold water in a beaker. Collect the insoluble material, heat it with some water in a test-tube, when it soon melts and sinks as dark-coloured drops. Decant off the water, add 2 c.c. of H_2SO_4 ; on heating a reddish colour develops.

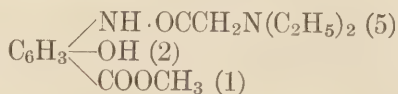
There are several derivatives of salicylic acid among the newer remedies, as **sanoform** or diiodomethyl salicylate, **salophen** or acetyl-paraminophenyl salicylate, and **salipyrin**, a combination of salicylic acid with antipyrin.

Orthoform is the methyl ester of aminohydroxy-

benzoic acid, $\text{C}_6\text{H}_3 \begin{cases} \text{NH}_2 \text{ (1)} \\ \text{—OH (2)} \\ \text{COOCH}_3 \text{ (4)} \end{cases}$. A *new* orthoform

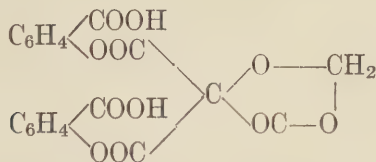
has been prepared in which OH is in position 3 instead of 2.

Anæsthesin has been proposed as a remedy to be used in the place of orthoform; it is the ethyl ester of para-amino benzoic acid. **Nirvanin** is the methyl ester of diethylglycocoll-aminosalicylic acid,



Aspirin is acetyl-salicylic acid, $\text{C}_6\text{H}_4 \begin{cases} \text{OOCCH}_3 \\ \text{—COOH} \end{cases}$.

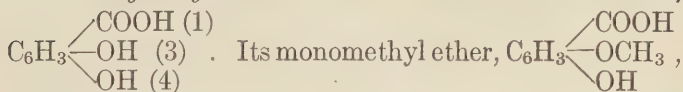
Novaspirin is a citric acid derivative,



Betol is the naphthol ester of salicylic acid,



B. *Dihydroxybenzoic acid*. **Protocatechuic acid**,

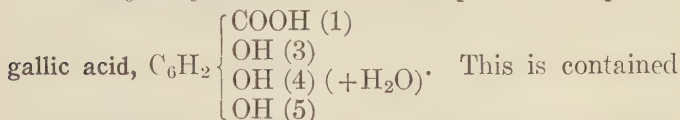


is vanillic acid, which is derived from vanillin, the corre-

sponding aldehyde, $\text{C}_6\text{H}_3 \begin{cases} \text{CHO} \\ \text{OCH}_3 \\ \text{OH} \end{cases}$, by oxidation. **Va-**

nilin, contained in the vanilla-bean, is extensively employed as a flavouring agent. It is used, with phloroglucin, as an indicator for free mineral acid (see p. 361), (Synthetically it can also be prepared by treating guaiacol, $\text{C}_6\text{H}_4 \begin{cases} \text{OCH}_3 \\ \text{OH} \end{cases}$, with chloroform and caustic soda.)

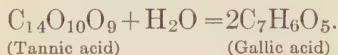
C. *Trihydroxybenzoic acid* is the important compound



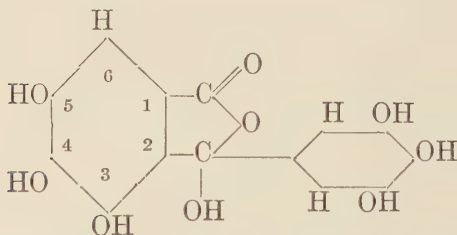
in certain plants, but is most readily obtained by boiling tannin with dilute mineral acid, or by fermenting gall-

nuts. **Tannic acid** (tannin), obtained from nutgall, consists of two molecules of gallic acid minus one molecule of water; it is therefore a condensation product.

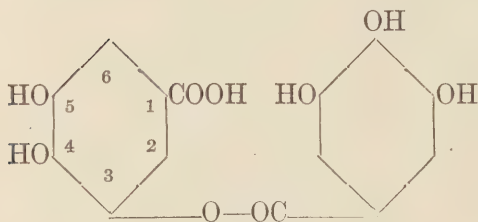
Tannic acid will be seen to bear a similar relation to gallic acid as disaccharides bear to monosaccharides:



The following structural formulæ have been proposed for tannic acid:

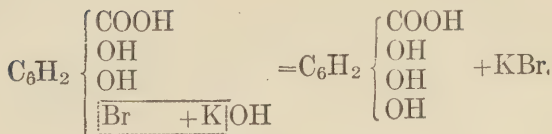


and



Its constitution is still under discussion.

That gallic acid has the structural formula given to it above is proved by the fact that it can be prepared by fusing bromprotocatechuic acid with KOH:



Gallic acid is almost insoluble in cold water, but soluble in hot water, alcohol, and ether, and its solutions give first a precipitate and then form a dark-green solution with ferric chloride. A *blue-black ink* is made by adding gallic acid to a slightly acid solution of ferrous sulphate to which indigo carmine has also been added. When this dries on paper it oxidizes, giving a heavy black precipitate. When distilled gallic acid yields pyrogallic acid and carbon dioxide (see p. 312). **Airol** and **dermatol** are combinations of gallic acid with bismuth.

Tannic acid is much more soluble than gallic. It gives the same reaction with ferric chloride. Tannic acid solution is dextrorotatory. It has a very extensive commercial use in tanning, in which process it forms insoluble and tough compounds with the protein, etc., in skin. It is also employed, on account of its astringent properties, in medicine. Many derivatives of tannic acid have been prepared as substitutes for it, such as **tannalbin**, **tannacol**, **tannigen**, **tannoform**, and **tannopin**, etc.

There are many substances of vegetable origin, similar in properties to tannic acid, but having different chemical structure. These are classed together as *tannins*. When acted upon by molten KOH some of these yield gallic acid, while others yield proto-catechuic acid. The tannin of tea and that of coffee is not identical with tannic acid.

EXPERIMENTS. (1) Test solutions of gallic acid and tannic acid with ferric chloride.

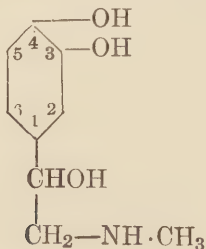
(2) Add tannic acid solution to some gelatin solution; the gelatin is precipitated.

(3) To a solution of quinine bisulphide (quinine dissolved in very dilute H_2SO_4) add tannic acid solution; the quinine is precipitated.

6. **Hydroxyl groups and fatty acid side chain.** **Tyrosin** is the chief representative. It is parahydroxyphenyl- α -aminopropionic acid, $\text{C}_6\text{H}_4\begin{matrix} \text{OH} \\ \diagup \\ \text{CH}_2 \cdot \text{CHNH}_2 \cdot \text{COOH} \end{matrix}$. Tyrosin is a decomposition product of protein. It gives a test with Millon's reagent. Proteins which contain no tyrosin (as gelatin, certain albumoses, etc.) do not give this test. It occasionally occurs in the urine as characteristic crystals. **Phenylalanin** is closely related to tyrosin, differing only in not being a hydroxy-acid; its formula is $\text{C}_6\text{H}_5 \cdot \text{CH}_2 \cdot \text{CHNH}_2 \cdot \text{COOH}$. **Homogentisic acid** has two hydroxyls; it is dihydroxyphenyl-

acetic acid, $\text{C}_6\text{H}_3\begin{matrix} \text{OH (5)} \\ \diagup \\ \text{OH (2)} \\ \diagdown \\ \text{CH}_2 \cdot \text{COOH (1)} \end{matrix}$. It has been found in the urine in cases of alcaptonuria, being derived from tyrosin and phenylalanin.

Adrenalin. This has the following structural formula.



Adrenalin (also called *suprarenin*) is the active principle in the extract from the suprarenal capsule, and when its solution is injected into the circulation of an animal several important effects are observed, chief of which is rise of blood-pressure. Adrenalin is optically active, $(\alpha)_D$ is -50.4 – -51.4° . *d. l.* Suprarenin has been prepared synthetically. By treating this with tartaric acid crystals can be obtained, from which *l* suprarenin is secured. This is found to be identical with natural adrenalin.

Epinephrin is said to be a derivative of adrenalin. By fusion with KOH suprarenin is converted into protocatechuic acid.

CHAPTER XXIX.

MIXED AROMATIC COMPOUNDS (*Continued*) (ALSO INDICATORS AND DYES.)

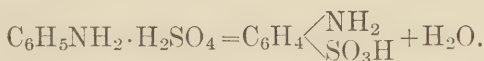
7. **Acid and nitro groups.** Benzoic acid readily reacts with nitric acid to form the nitrobenzoic acids. The meta variety is formed in greatest amount. As already pointed out, nitrobenzoic acids may also be obtained by oxidizing the corresponding nitrotoluenes (see p. 328).

8. **Acid and amino groups.** By reducing the nitro, benzoic acids with tin and hydrochloric acid (nascent hydrogen) amino derivatives of benzoic acid may be obtained (*cf.* reduction of nitrobenzene to aniline, p. 329). The ortho variety of these is known as *anthranilic acid*, $\text{C}_6\text{H}_4 \begin{smallmatrix} \text{COOH} \\ \text{NH}_2 \end{smallmatrix}$. It is produced as an intermediate product in the preparation of aniline by boiling indigo with caustic alkali.

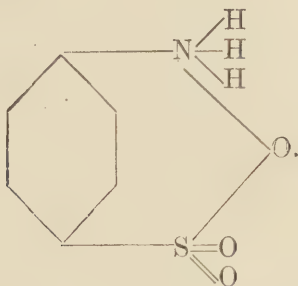
9. **Acid and sulpho groups.** Metasulphobenzoic acid is produced by the action of sulphuric acid on benzoic acid. The important substance **saccharin** is the imide of orthosulphobenzoic acid, $\text{C}_6\text{H}_4 \begin{smallmatrix} \text{CO} \\ \text{SO}_2 \end{smallmatrix} \text{NH}$, and is also called benzosulphinide. It is intensely sweet, and

antiseptic; on account of these properties it is used as a medicine and a preservative.

10. **Sulphonic and amino groups.** By the action of sulphuric acid on aniline, aniline sulphate is first of all formed and then becomes converted into paraminobenzenesulphonic acid or **sulphanilic acid**, $\text{C}_6\text{H}_4\begin{smallmatrix} \text{NH}_2 \\ \text{SO}_3\text{H} \end{smallmatrix}$, by dehydration:



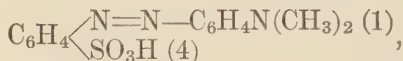
In sulphanilic acid it has been supposed that the amino and sulpho side chains are linked together through an oxygen atom so as to form an inner salt, thus:



Sulphanilic acid is soluble in hot water, but only sparingly so in cold water. Its solutions are acid in reaction, thus differing from taurin (aminoethyl-sulphonic acid, see p. 217). It is used in the manufacture of dyes, in a large number of which there exists the sulphonic acid group along with a diazo group. Two of these dyes, viz., **methyl orange** and **tropæolin OO**, are used as indicators in bio-chemistry.

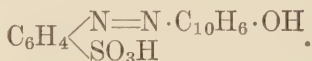
EXPERIMENT. *Preparation of sulphanilic acid.* To 50 gm. of C.P. H_2SO_4 in a flask, add gradually 15 c.c. of aniline, and heat in an oil-bath at 180° – 190° for about four hours, until a test-drop, diluted with water and treated with NaOH , shows no unchanged aniline. Cool, and pour into a beaker of cold water while stirring the latter. Filter off the crystals. Evaporate the filtrate to small volume to secure more crystals. Recrystallize from hot water.

Helianthin is dimethyl-aminoazobenzene-sulphonic acid,



prepared by acting on benzene-diazonium-sulphonic acid with dimethylaniline. Its sodium salt is *methyl orange* (see indicators, p. 360).

Orange II is an azo dye, somewhat related to methyl orange in chemical structure:



EXPERIMENT. Dissolve 10 gm. of dry sulphanilic acid in 100 c.c. of 2.5% Na_2CO_3 solution (made with anhydrous carbonate), and add 3.5 gm. of NaNO_2 dissolved in 20 c.c. of water. Cool with ice-water, gradually add diluted HCl (6 c.c. + 10 c.c. H_2O), and finally add an acid solution of dimethylaniline (6 gm. + 6 c.c. HCl + 20 c.c. H_2O). Render the mixture alkaline with NaOH solution and add 20 gm. of NaCl . Filter off the methyl orange precipitate and crystallize from hot water. To a little dilute solution of methyl orange add

some acid -a red colour is obtained. Save a sample of the crystals.

Tropæolin OO is diphenyl-aminoazobenzene-sulphonic acid, C_6H_4 $\begin{cases} \text{N}_2-\text{C}_6\text{H}_4\text{NHC}_6\text{H}_5 \\ \text{SO}_3\text{H} \end{cases}$. Its alcoholic

solution gives a violet colour with free mineral acid; or, if its alcoholic solution be evaporated to dryness, the resulting residue, while still warm, gives a violet colour with free mineral acids. Applied in this latter manner the test is very delicate. It is thus used as an indicator in analysis of the gastric juice.

INDICATORS.

At this stage it will be convenient to discuss briefly the **theory of the action of indicators**.

These must possess weak acid or basic properties, and be, therefore, undissociated when in a free state, but dissociated when present as salts. In the dissociated state the anion must have a different colour from that of the undissociated compound.

Taking the three most commonly used indicators, phenolphthalein, methyl orange, and litmus, let us see in how far their actions can be thus explained.

(1) *Phenolphthalein*. This is of the nature of a very feeble acid, so that it is undissociated when in a free state, and when undissociated it is colourless. When dissociated, however, its anion has a red colour. Dissociation occurs when it is converted into a salt. Thus, when we titrate an acid with sodium hydroxide, using phenolphthalein as indicator, what happens is this: In the presence of the acid the phenolphthalein is undis-

sociated, and the solution is therefore colourless; as alkali is added the acid becomes gradually neutralized, until at last a trace of alkali in excess of that necessary to neutralize the acid is present; this trace combines with the phenolphthalein, forming a salt which then dissociates, so that the anion imparts its red colour to the solution.

The acid to be titrated must be distinctly stronger than phenolphthalein, for otherwise, before the former has all been neutralized, some of the salt formed will become hydrolyzed, and the base thus liberated will combine with the phenolphthalein and form a salt which, partially dissociating, will impart a pink tint to the solution. Thus, phenols cannot be titrated with phenolphthalein. On the other hand, such a feeble acid as carbonic is so much stronger than phenolphthalein that the latter can be employed as an indicator for titrating it. On this account carbon dioxide (carbonates) must be absent from the standard alkali used for titrating. Phenolphthalein can also be used for practically all organic fatty acids.

The base used for neutralization must also be a strong one. Thus, if a feeble base such as ammonia be employed, then the salt which it forms with the phenolphthalein will be so feeble that it will be decomposed by the water (hydrolysis), and the end reaction will be indefinite, an excess of ammonia requiring to be present before the decomposing effect of the water is overcome. Phenolphthalein must not, therefore, be used when ammonia or ammonium salts are present in a solution.

Phenolphthalein is the ideal indicator for weak acids

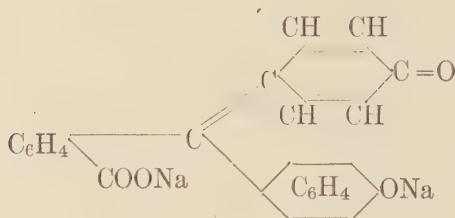
and acid salts, and should be employed along with a strong strong base.

(2) *Methyl Orange*. This is the sodium salt of a much stronger acid than phenolphthalein, and it dissociates readily in weak solution. When undissociated it is red, when dissociated its anion is yellow. Its dissociation in water is prevented by the presence of a trace of stronger acid,—such solutions are therefore red,—but if alkali be added in sufficient amount just to neutralize this acid, then the methyl orange partially dissociates and the solution becomes much paler, and if a trace more alkali be added still more dissociation occurs, so that the solution becomes bright yellow. Methyl orange is not affected by acid sodium phosphate (NaH_2PO_4), so that a weak acid such as this must be present in large excess before it can prevent the dissociation of methyl orange, therefore for titrating acid salts this indicator is unsuitable; for the same reasons it cannot be used for weak organic acids. On the other hand, it is suitable for practically all bases and carbonates, since with all of them it will immediately form dissociable salts, which do not hydrolyze so long as any of the base is available (i.e., uncombined with the acid that is being titrated, which must, of course, be stronger than methyl orange). Nitrous acid acts on methyl orange chemically.

Methyl orange is therefore especially useful for the titration of bases, including ammonia, and unsuitable for the weaker organic acids.

According to a recent theory the colour change of phenolphthalein and methyl orange is due to intramolecular rearrangement and production of a tautomer

having a quinoid structure (a CH group of benzene changed to CO). For example, the red salt of phenolphthalein (in the presence of alkali) is said to have the following quinoid formula:



Compare the formula of phenolphthalein (p. 326).

The indicators used for the detection of mineral acid in the gastric contents belong to the same class as methyl orange, e.g., *Congo red* (p. 369) and *dimethyl-amidoazobenzene* (p. 337).

While it is true that these indicators will not give an accurate titration value with organic acids, our experience (contrary to statements in clinical chemistry textbooks) is that methyl orange, Congo red, and dimethyl-amidoazobenzene give a distinct colour reaction (as with mineral acids) even when used with very dilute organic acid solutions; for example, a $\frac{\text{N}}{286}$ lactic acid solution (1 drop of pure acid in 100 c.c. of water) reacts acid to these indicators. The phloroglucin-vanillin reagent (p. 312), however, reacts only to mineral acid and can be used as the indicator when making a quantitative estimation of mineral acid in the presence of organic acids.

(3) *Litmus*. This stands between phenolphthalein and methyl orange in its properties. In the un-ionized state it is red, therefore red with acids; and in the ionized state blue, therefore blue with alkalis.

The importance to the student of thoroughly understanding the action of these three indicators will be evident from the fact that the blood and urine react very differently towards them. Towards methyl orange both blood and urine (even when the latter is acid to litmus) react alkaline or neutral, towards phenolphthalein they react acid, while towards litmus blood reacts alkaline and urine (usually) acid. The cause of this difference in action lies in the fact that in both of these animal fluids we have a mixture of NaH_2PO_4 and Na_2HPO_4 . Occasionally these two salts are present in equivalent quantities in the urine (normally in milk also); in such a case the urine reacts acid to blue litmus and alkaline to red litmus (amphoteric reaction). This is due to the fact that NaH_2PO_4 is acid to litmus and Na_2HPO_4 is alkaline. In normal (acid) urine NaH_2PO_4 preponderates over the alkaline salt, therefore the urine reacts acid to litmus; in shed blood, however, Na_2HPO_4 is present in excess, therefore it reacts alkaline to litmus. Both of these, even the acid-reacting NaH_2PO_4 , are but feebly dissociated (i.e., furnish few ions) compared with the relatively strong acid in methyl orange; therefore they are unable to influence the degree of dissociation of methyl orange. Congo red acts in the same manner as methyl orange. Phenolphthalein, however, is so feeble an acid that both of these acid salts can readily keep it in the (practically) undissociated condition, and do not allow it to form its sodium salt, under which circumstances, as we have already stated, it remains colourless.

EXPERIMENTS. (1) Effect of ammonium salts on indicators. (a) Titrate 5 c.c. of decinormal H_2SO_4 containing ammonium sulphate with decinormal NaOH ,

using methyl orange as indicator. (b) Repeat (a) but use phenolphthalein as indicator.

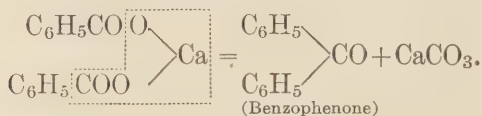
(2) Organic acids. (a) Titrate 5 c.c. of decinormal butyric acid with methyl orange; (b) with phenolphthalein.

(3) Acid salts (a) Titrate 5 c.c. of dilute NaH_2PO_4 solution, using phenolphthalein as indicator. (b) With litmus paper (both blue and red) test solutions of NaH_2PO_4 and Na_2HPO_4 , then mix equal volumes of corresponding solutions of the two phosphates, and test with litmus (amphoteric).

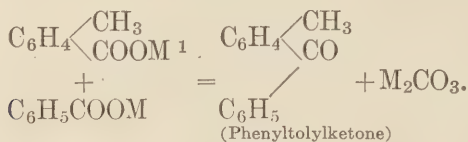
11. **Ketone group (CO) with two phenyl groups** (aromatic ketones), or linking together of a phenyl and fatty group (mixed aromatic fatty ketones).

These are prepared by methods analogous with those already studied in connection with aliphatic ketones, thus:

a. By distilling calcium benzoate, diphenyl ketone or *benzophenone* is produced:

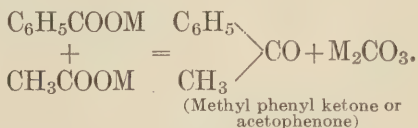


b. By distilling salts of two different aromatic acids, such as a salt of benzoic and one of toluic acid:



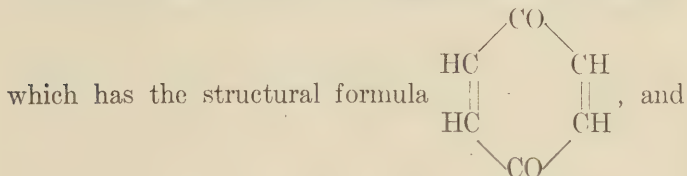
¹ The salt usually employed is that of calcium. M means a metal.

c. By distilling a salt of an aromatic acid with one of a fatty acid:



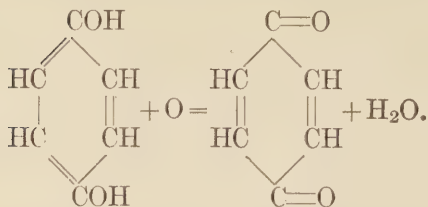
Acetophenone may also be obtained by adding aluminium chloride to a mixture of benzene and acetyl chloride. It is a crystalline substance melting at 20.5° , and is slightly soluble in water. It is used in medicine as a hypnotic under the name of *hypnone*.

Quinones. These may be regarded as diketones.¹ The best known of them is **benzoquinone** or *quinone*,



may be prepared by oxidizing various para derivatives of benzene, but not ortho or meta derivatives. Thus *p*-phenolsulphonic acid, *p*-sulphanilic acid, *p*-amido-phenol, etc., all yield quinone when oxidized. It is usually prepared, however, by oxidizing aniline with chromic acid or by oxidizing hydroquinol:

¹ These do not strictly belong to the class of bodies that we are considering as mixed compounds.



These reactions for its preparation (with the exception of its preparation from aniline) leave little doubt as to its structural formula.

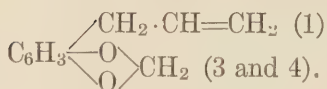
The quinones are of a yellow colour and possess a pungent odour. They have oxidizing properties and are important in dye chemistry.

Several dyes have already been mentioned. All such bodies are supposed to owe their dyeing properties to the presence in them of a so-called *chromophore group*. Chromophore groups are of various kinds, of which the following are important:

1. The azo group $\text{N}=\text{N}$, as in orange II (see p. 357).
2. The nitro group NO_2 , as in picric acid (see p. 306).
3. The group $\text{C}(\text{R})=\text{N}$, as in methyl violet (see p. 332).
4. The group $(\text{R})\langle \begin{array}{c} \text{CO} \\ \diagup \quad \diagdown \\ \text{CO} \end{array} \rangle (\text{R})$, as in alizarin (see p. 371).

The presence in a substance of one of these groups alone is not, generally, sufficient to constitute it a dye; certain other groups, such as OH and NH_2 , must, as a rule, be attached to a chromophore-containing compound to render it available as a dye. These assisting or auxiliary groups are called *auxochromes*. The chemistry of the cause of colour in organic compounds is being vigorously investigated; as a result it will

oil. It is the methylene ether of allyl pyrocatechol.

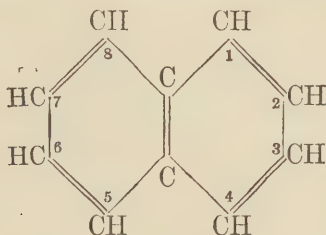


Apiol has the same formula as safrol, except that it has OCH_3 groups in the place of H in positions 2 and 5.

CHAPTER XXX

AROMATIC COMPOUNDS HAVING CONDENSED RINGS.

Naphthalene ($C_{10}H_8$) contains two benzene rings connected together in the following manner:



It forms white crystals melting at 79.6° , boiling at 218.1° and having a tar-like odour. It is volatile and is contained in coal-gas, being also a constituent of the distillate from coal-tar.

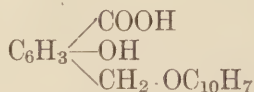
EXPERIMENTS. (1) Heat some naphthalene in a sublimation apparatus.

(2) Try the reaction with aluminium chloride given by some naphthalene dissolved in chloroform (see p. 296).

The **naphthols**, $C_{10}H_7 \cdot OH$, correspond to phenols. Alpha-naphthol (melting-point 95°) and beta-naphthol (melting-point 122°) are both of importance. α Derivatives of naphthalene have some group introduced in position 1, 4, 5 or 8, while β derivatives have it in

position 2, 3, 6 or 7. Ortho, meta and para naphthalene derivatives have two substituting groups attached to the same half of the formula (as in positions 1, 2, 3, 4).

Epicarin is β -naphthol-ortho-hydroxy-toluic acid,



β -naphthol benzoate, $\text{C}_{10}\text{H}_7\text{—OOC} \cdot \text{C}_6\text{H}_5$, is another of the newer remedies.

Orphol is a combination of beta-naphthol with bismuth nitrate. All these substances are antiseptics. *Alpha- and beta-naphthylamines*, $\text{C}_{10}\text{H}_7 \cdot \text{NH}_2$, are used as reagents.

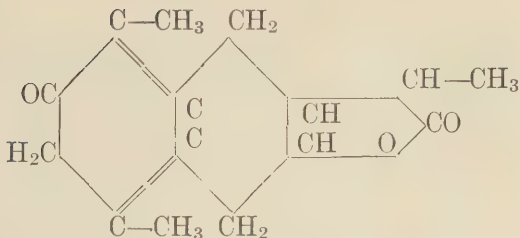
α -Naphthylamine is used to detect the presence of and to estimate the amount of traces of nitrites, as in drinking water. This test depends on the fact that a red compound, azo-benzene-naphthylamine-sulphonic acid, is produced.

Congo red is a complex diazonium derivative of naphthylamine-sulphonic acid. Its formula is



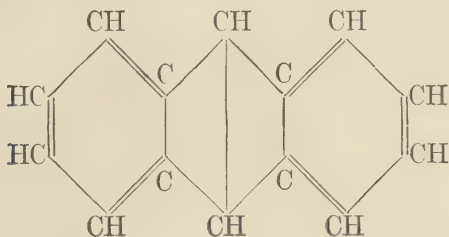
Its colour becomes blue in the presence of free acids. It forms a colloidal solution, which will not dialyze. Electrolytes cause its molecules to aggregate.

Santonin, $\text{C}_{15}\text{H}_{18}\text{O}_3$, is a derivative of naphthalene and is the anhydride or lactone of santoninic acid. Its formula is probably,

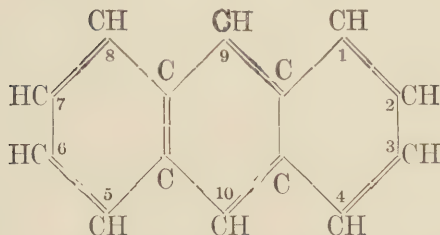


Elaterin, a neutral principle, is said to be a derivative of naphthalene.

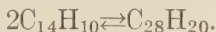
Anthracene. $C_{14}H_{10}$, is a hydrocarbon containing three benzene rings condensed together:



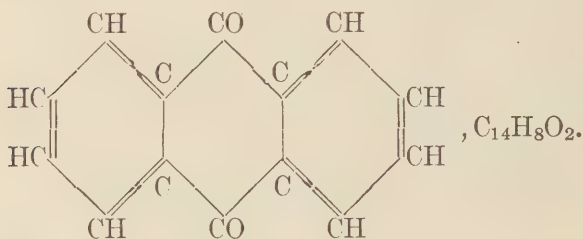
or



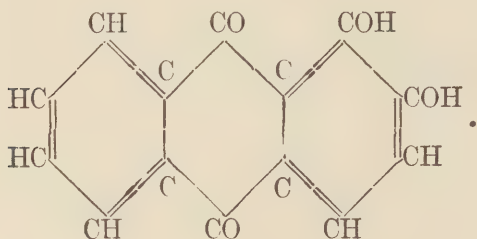
It occurs in coal-tar in small quantity and is used in manufacturing alizarin. Its crystals melt at 216.5° (corrected). Exposure to light changes it into dianthracene, this depolymerizes in the dark to anthracene, a reversible photo-chemical reaction:



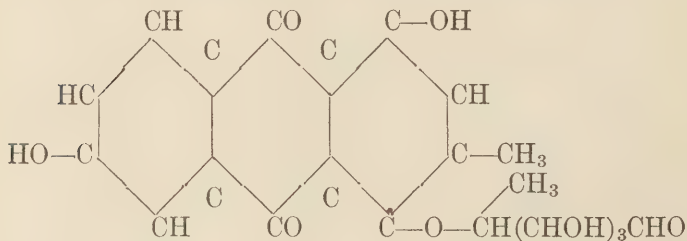
One of the important derivatives of anthracene is **anthraquinone**,



Dihydroxyanthraquinone is the very important dye **alizarin**, $C_{14}H_6O_2(OH)_2$:



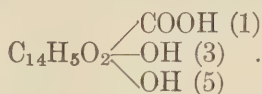
Aloin is an anthraquinone derivative, its formula may be (the position of the OH being uncertain):



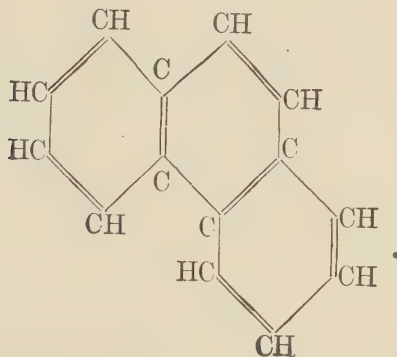
Chrysophanic acid, $C_{14}H_5O_2(CH_3)(OH)_2$, and **chrysarobin**, $C_{15}H_{12}O_3$, are anthracene derivatives of therapeutic importance, chrysophanic acid probably being monomethyl-dihydroxy-anthraquinone, and chrysarobin monomethyl-trihydroxy-anthracene.

Emodin, $C_{15}H_{10}O_5$, is a 2-monomethyl 3, 6, 7-trihydroxyanthraquinone.

Rhein, $C_{15}H_8O_6$, is also an anthraquinone derivative,



Isomeric with anthracene is **phenanthrene**, $C_{14}H_{10}$:

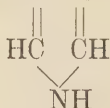


CHAPTER XXXI.

HETEROCYCLIC COMPOUNDS.

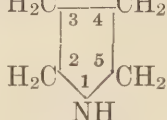
HETEROCYCLIC compounds are related to the aromatic compounds, but contain at least one atom other than C atoms in the ring; this is generally N.¹

Pyrrol has the formula HC—CH. *Iodol* is a medicinal



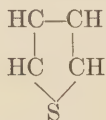
derivative, it is tetraiodopyrrol.

Pyrrolidine is the hydrogen addition derivative of pyrrol, H₂C—CH₂. This is the basis of certain alkaloids.

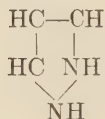


Prolin and hydroxy-prolin are pyrrolidine acids (p. 216).

¹ Heterocyclic compounds of minor importance are thiophene,

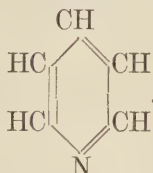


and pyrazole,



Hæmatin, hæmin, and hæmatoporphyrin (from hæmoglobin) are supposed to contain four pyrrol rings in their molecules.

Pyridine Bases. These are ammonia derivatives and of great importance on account of their relationship to certain alkaloids which will be discussed presently. The simplest member of the series is pyridine, which has the

structural formula . It may therefore be

considered as benzene with a CH group replaced by nitrogen (C_5H_5N). There are several methyl pyridines.

The pyridines are contained in coal-tar, and are formed when bones are distilled, being produced by the action on one another at high temperatures of acrolein, ammonia, methylamine, etc.

Pyridine is a colourless liquid with an odour like tobacco-smoke. It boils at $115^\circ C$. It mixes readily with water, the resulting solution being strongly alkaline. Like other tertiary ammonia bases, it directly combines with acids to form crystalline salts. When warmed with alkyl halides addition products are formed, and if these be treated with caustic potash a very pungent and disagreeable odour is evolved.

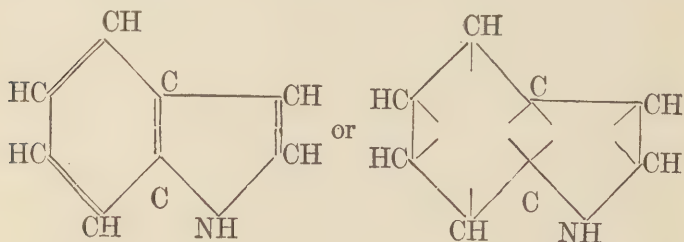
EXPERIMENTS. (1) Dissolve some pyridine in water; test alkalinity with litmus. Notice the odour.

(2) Then neutralize the solution with HCl, add a few drops of platinic chloride solution, and boil; a yellow precipitate of $(C_5H_5N)_2PtCl_4$ forms.

CONDENSED HETEROCYCLIC BENZENE COMPOUNDS.

PYRROL DERIVATIVES OF BENZENE.

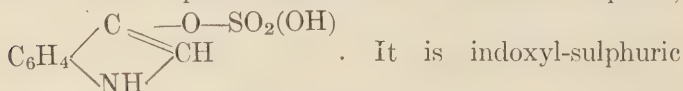
Indol, $C_6H_4 \begin{smallmatrix} \diagup CH \\ \diagdown NH \end{smallmatrix} \diagup CH$, contains the pyrrol nucleus, condensed with the benzene nucleus, and may be represented thus:



Skatol is methyl indol, $C_6H_4 \begin{smallmatrix} \diagup C \\ \diagdown NH \end{smallmatrix} \diagup CH$. Indol

and skatol are contained in faeces, imparting the characteristic odour to the latter. They are produced in the intestine by the action of bacteria on the aromatic groups (tryptophan) in protein. They are volatile with steam.

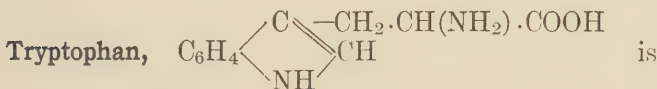
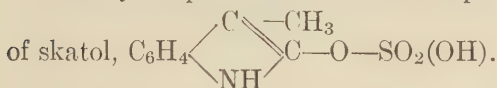
Indican is the oxidation product of indol in combination with sulphuric acid as an ethereal sulphate,



It is indoxyl-sulphuric acid. It is sometimes present as a potassium salt in the urine in considerable quantity. The urine may also contain indoxyl glycuronic acid. The origin of these bodies is indol absorbed from the bowel-contents.

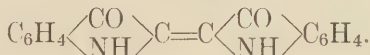
Indigo can be obtained from it, and occasionally indigo is deposited from urine containing much indican after ammoniacal decomposition sets in. To estimate the indican in the urine it is converted into indigo by various reagents, and this is then removed by shaking with chloroform. The blue chloroform solution can be compared with an indigo solution of known strength, and thus a colourimetric estimation may be made.

Skatoxyl-sulphuric acid is the corresponding derivative



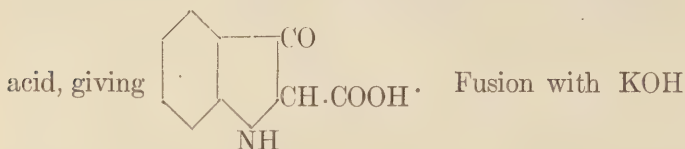
β -indol α -amino-propionic acid. It is a decomposition product of protein, being produced during tryptic digestion. It, in turn, is attacked by bacteria, giving rise to indol. It gives a colour reaction with glyoxylic acid (see p. 204).

Directly related to indol is **isatin**, $\text{C}_6\text{H}_4 \begin{array}{c} \diagup \text{CO} \diagdown \\ \diagdown \text{NH} \diagup \end{array} \text{CO}$, dioxyindol, for the former can be obtained from the latter by reduction. **Indigo**, structurally, is a combination of two isatin molecules, the end oxygen atom of each molecule being eliminated, thus:



Indigo can be produced from isatin. It is a valuable blue dye. The synthesis of indigo on a commercial scale is one of the great achievements of chemistry.

Most of the indigo marketed nowadays is artificially produced, the cost of manufacture being only about one-fourth the cost of production of natural indigo. Naphthalene is the starting-point of the synthesis. This is oxidized by fuming H_2SO_4 to phthalic acid, the latter is converted into phthalimide, by treatment with chlorine and soda; this becomes anthranilic acid. This acid is condensed with chloracetic



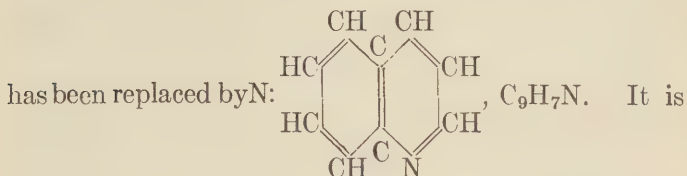
converts this into indoxyl, and the latter is oxidized to indigo by exposure to the air.

In plants the indigo is contained in a glucoside combination. Reduction (adding H) changes indigo to *indigo white*; it is in this form that it is introduced into cloth for dyeing. Indigo red, *indirubin*, is a structural isomer of indigo.

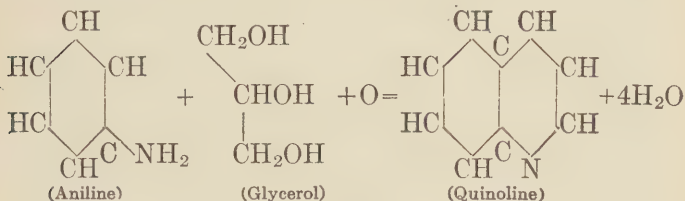
EXPERIMENT. Synthesize indigo. To 1 c.c. of water add 3 drops of acetone and a few crystals of ortho-nitrobenzaldehyde, warm the mixture in a bath kept at 50° for ten minutes. Cool, add a few drops of 10% NaOH and shake. A yellow colour appears first, then a green. When deep green add chloroform and shake. Indigo dissolves in the chloroform (blue solution). Remove the bottom layer with a pipette, and run it into a sample bottle. As the solvent evaporates indigo is deposited on the wall.

CONDENSED PYRIDINE-BENZENE COMPOUNDS.

Quinoline (chinoline) is another tertiary ammonia base. It may be considered as naphthalene in which a CH group



found in coal-tar. When certain alkaloids, particularly quinine and cinchonine, are distilled with potassium hydroxide, quinoline is obtained. Quinoline can be synthesized from aniline and glycerol in the presence of nitrobenzene and concentrated sulphuric acid (see exp. below):



Quinoline is a liquid boiling at 237° . By proper treatment of quinoline, pyridine can be derived from it. Many alkaloids are quinoline derivatives.

Oxyquinoline Sulphate (chinosol), $(C_9H_7NO)_2 \cdot H_2SO_4$, is a substance used as an antiseptic, and is said to be non-toxic.

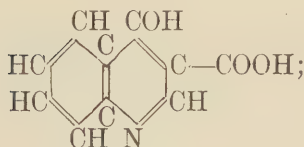
EXPERIMENT. *Synthesize quinoline.* In a litre flask mix 15 gm. of nitrobenzene, 24 gm. of aniline, and 75 gm. of glycerol; add 62 gm. of C.P. H_2SO_4 while agitating the mixture. Connect with an air-condenser having a diameter of 2 cm., and heat the flask very gradually on a sand bath. Wrap the condenser with a damp rag. When the reaction begins (sudden bubbling) remove the flame. If the action is very vigorous, cool the upper part of the flask with an air stream from a bellows. When the mixture becomes quiet, heat for three hours on a sand bath. Then dilute with 300 c.c. of water and distil with steam. When no more oily drops of nitrobenzene come over, stop the distilling. Cool partially, render the mixture alkaline with strong NaOH solution, and again distil with steam, thus removing the quinoline and aniline. This last distillate is specially treated to convert the aniline into phenol, as was directed in the experiment under phenol (see p. 259). Diazotize the cooled liquid after rendering it distinctly acid with dilute H_2SO_4 , warm in a bath, make alkaline (the phenol becomes fixed as a phenolate, while quinoline is set free), and distil with steam. Extract the quinoline from the distillate with ether and proceed just as was done with phenol.

Thalline, $\text{C}_9\text{H}_9(\text{OCH}_3)\text{NH}$, and

Kairine, $\text{C}_9\text{H}_9(\text{OH})\text{N}-\text{C}_2\text{H}_5$, are quinoline derivatives that have been used as antipyretics.

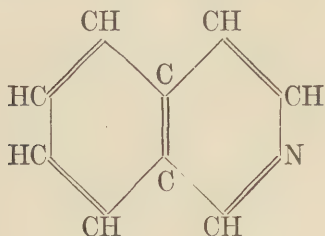
Analgen (quinalgen) is a more recent antipyretic, $\text{C}_9\text{H}_5(\text{OC}_2\text{H}_5)\text{NH}(\text{COC}_6\text{H}_5)\text{N}$.

Kynurenic acid, occurring in the urine of dogs, is a quinoline derivative,



it is supposed to be derived from tryptophan.

Isoquinoline, C_9H_7N , is an isomer of quinoline:



It is of importance because of the derivation of many alkaloids from it. The formula may be written with N at any one of the four positions at the sides of the rings.

SYNOPSIS.

Aromatic Compounds.

A. BENZENE HYDROCARBONS.

Benzene derivatives.

1. *Halogen derivatives.*

2. *Hydroxy derivatives.*

a. Phenols { Ethers.
Ethereal salts.

(1) Monacid phenols { Substitution
products.

(2) Diacid phenols.

(3) Triacid phenols.

(4) Hexacid phenol derivative.

b. Fatty alcohol side-chain compounds and deriva-

tives { Alcohols (primary).
Aldehydes.
Monobasic acids { Salts.
Ethereal salts.

3. Dibasic acids.**4. Nitrogen derivatives.**

(a) Nitro compounds.

(b) Amino compounds.

(c) Diazo compounds.

5. Sulphur derivatives.**6. Mixed compounds.**

(1) Phenol and sulphonic groups.

(2) Phenol and nitro groups.

(3) Phenol and amino groups.

(4) Phenol and primary alcohol groups.

(5) Hydroxy-acids.

(6) Hydroxyl groups and fatty acid side chain.

(7) Acid and nitro groups.

(8) Acid and amino groups.

(9) Acid and sulpho groups.

(10) Sulphonic and amino groups.

(11) Ketone linkings and quinones.

(12) Unsaturated side-chain combinations with benzene derivatives.

B. CONDENSED BENZENE RINGS.1. *Naphthalene*.2. *Anthracene*.3. *Phenanthrene*.**C. HETEROCYCLIC COMPOUNDS.**1. *Pyrrrol and pyridine bases*.2. *Condensed heterocyclic-benzene rings*.

(1) Indol and derivatives.

(2) Quinoline and derivatives.

(3) Isoquinoline and derivatives.

(4) Alkaloids.

CHAPTER XXXII.

ALKALOIDS AND DRUG PRINCIPLES.

ALKALOIDS.

IN its broadest application the term alkaloid includes all nitrogenous organic substances that are basic in character (*alkaloid* = *alkali-like*). Caffeine and theobromine, purin bases and other leucomaines, choline, muscarine, and other ptomaines are all called alkaloids.

Most alkaloids are tertiary ammonia bases. The most recent definition which seems acceptable is that alkaloids include all nitrogenous plant products which have N in a closed chain of atoms. Those whose structure is known are derivatives of pyridine, pyrrolidine, quinoline, isoquinoline, phenanthrene or purin.

The empirical formulæ of the chief alkaloids are as follows:

Coniine	$C_8H_{17}N$.
Nicotine	$C_{10}H_{14}N_2$.
Sparteine	$C_{15}H_{26}N_2$.
Theobromine	$C_7H_8N_4O_2$.
Theophylline	$C_7H_8N_4O_2$.
Caffeine	$C_8H_{10}N_4O_2$.
Pelletierine	$C_8H_{15}NO$.
Pilocarpidine	$C_{10}H_{14}N_2O_2$.
Hydrastinine	$C_{11}H_{13}NO_3$.

Pilocarpine	$C_{11}H_{16}N_2O_2$.	
Physostigmine	$C_{15}H_{21}N_3O_2$ (Eserine).	
Eseridine	$C_{15}H_{23}N_3O_3$.	
Homatropine	$C_{16}H_{21}NO_3$.	
Sinipine	$C_{16}H_{25}NO_6$.	
Apomorphine	$C_{17}H_{17}NO_2$.	
Piperine	$C_{17}H_{19}NO_3$.	
Morphine	$C_{17}H_{19}NO_3$.	
Cocaine	$C_{17}H_{21}NO_4$.	
Hyoscyne	$C_{17}H_{21}NO_4$ (Scopolamine).	
Atropine	$C_{17}H_{23}NO_3$	} Isomers.
Hyoscyamine	$C_{17}H_{23}NO_3$	
Codeine	$C_{18}H_{21}NO_3$.	
Lobeline	$C_{18}H_{23}NO_2$.	
Thebaine	$C_{19}H_{21}NO_3$.	
Cinchonine	$C_{19}H_{22}N_2O$	} Isomers.
Cinchonidine	$C_{19}H_{22}N_2O$	
Curarine	$C_{19}H_{26}N_2O$.	
Sanguinarine	$C_{20}H_{15}NO_4$.	
Berberine	$C_{20}H_{17}NO_4$.	
Papaverine	$C_{20}H_{21}NO_4$.	
Quinine	$C_{20}H_{24}N_2O_2$ (Isomer, Quinidine)	
Hydrastine	$C_{21}H_{21}NO_6$.	
Strychnine	$C_{21}H_{22}N_2O_2$.	
Narcotine	$C_{22}H_{23}NO_7$.	
Colchicine	$C_{22}H_{25}NO_6$.	
Gelseminine	$C_{22}H_{26}N_2O_3$.	
Yohimbine	$C_{22}H_{28}N_2O_3$.	
Brucine	$C_{23}H_{26}N_2O_4$.	
Narceine	$C_{23}H_{27}NO_8$.	
Jervine	$C_{26}H_{37}NO_3$.	
Emetine	$C_{30}H_{40}N_2O_5$	

Veratrine.....	$C_{32}H_{49}NO_9$.
Aconitine.....	$C_{34}H_{47}NO_{11}$.
Ergotinine.....	$C_{35}H_{39}N_5O_5$.
Ergotoxine.....	$C_{35}H_{41}N_5O_6$.

Coniine and nicotine are the only important alkaloids that contain no oxygen and that are volatile liquids. Sparteine, pelleteirine and pilocarpidine are liquids, but non-volatile. All of the alkaloids form salts with acids (see p. 187); these salts are very much more soluble in water and alcohol than the free alkaloids. The free alkaloids, on the other hand, are more soluble than their salts in the immiscible solvents—ether, chloroform, benzene, and amyl alcohol.

All alkaloids are precipitated by phosphomolybdic and phosphotungstic acids, most of them by potassium mercuric iodide and many of them by tannic acid.

Most of the alkaloids are optically active, generally lævorotatory.

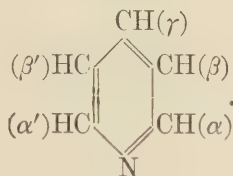
Many of the alkaloids are extremely poisonous, but in minute doses they are very valuable remedies.

The alkaloids here considered are of vegetable origin, practically all coming from dicotyledonous plants.

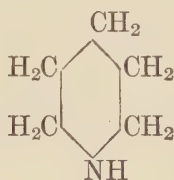
We shall consider now some of the facts that are known in regard to the structure of alkaloids.

PYRIDINE DERIVATIVES.

It is necessary to designate the positions of groups in the pyridine ring thus:

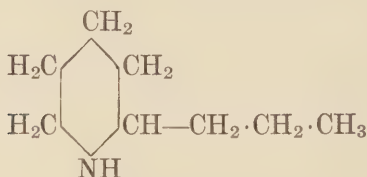


Piperidine is the simplest derivative,

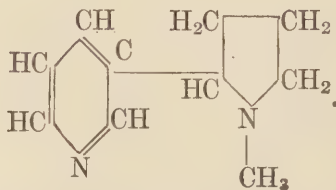


Piperine is contained in pepper. It is a combination of piperidine and piperinic acid.

Coniine is dextro- α -propyl piperidine,



Nicotine is a pyrrol derivative (see p. 373) of pyridine the attachment of methyl pyrrolidine to pyridine being in the β position of the latter and position 2 of the former:



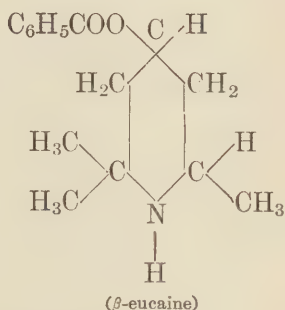
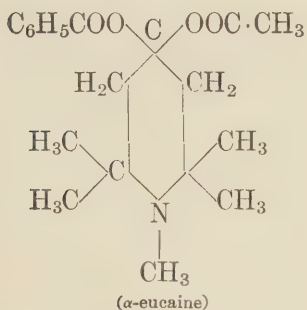
Coniine and nicotine have marked similarities; both are volatile liquids having a strong odour, and both are very poisonous. Coniine is obtained from hemlock-seed, and nicotine from tobacco. Both are strongly alka-

line to litmus. In tobacco the nicotine is combined with malic acid and citric acid. Synthetic α -propyl piperidine is identical with coniine, except that it is optically inactive. Optically active coniine can be obtained from this by securing crystals of the tartrate of coniine, the first crop of crystals containing only dextroconiine. This was the first synthesis (1886) of a natural alkaloid.

Nicotine is lævorotatory. *d l*-Nicotine has been synthesized; from this the *l* variety is separated by crystallization of the tartrate. *d*-Nicotine is much less toxic than *l*-nicotine.

Sparteine is thought to be a piperidine derivative, but its chemical structure has not been fully determined. It is dextrorotatory.

The artificial alkaloids α - and β -**eucaine** are complex piperidine bodies.



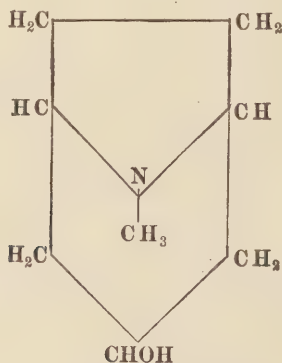
The eucaines are local anæsthetics, and differ from cocaine in action in that they do not affect the pupil.

Euphthalmine is related to β -eucaine, having a CH_3 group in place of the H attached to N and having the

mandelic acid radicle, $C_6H_5 \cdot CHO \cdot COO$ instead of the benzoic acid radicle. It dilates the pupil more quickly and less persistently than atropin. It is not an anæsthetic.

PYRROLIDINE DERIVATIVES.

The alkaloids of the cocaine and atropine group are all pyrrolidine derivatives. This class of alkaloids is of great pharmacological importance. Cocaine is an invaluable local anæsthetic, while members of the atropine group are used to dilate the pupil. The basal substance for all of these compounds is tropine. This has, as will be noticed, a secondary closed carbon chain:

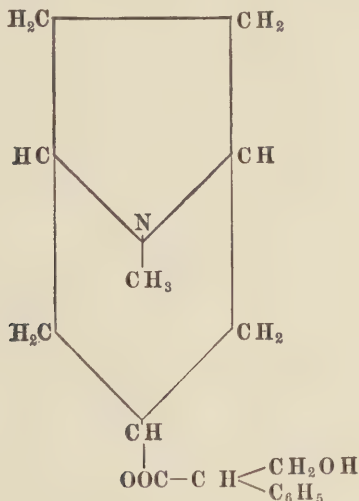


This double ring nucleus is called the tropane nucleus. It may be looked upon as a condensation of the pyrrol with the pyridine ring, having N and the two neighboring C atoms in common to the two rings.

Tropic acid has the formula



Atropine is the tropine ester (tropine being an alcohol) of tropic acid, its formula being



Atropine is optically inactive. Its physiological action is what would be expected of *d l*-hyoscyamine. **Hyoscyamine** is lævorotatory. *d*-Hyoscyamine has a different degree of physiological action. Like other esters, atropine and hyoscyamine can be saponified. Atropine has been synthesized.

Atropine and its isomers have a marked pharmacological action.

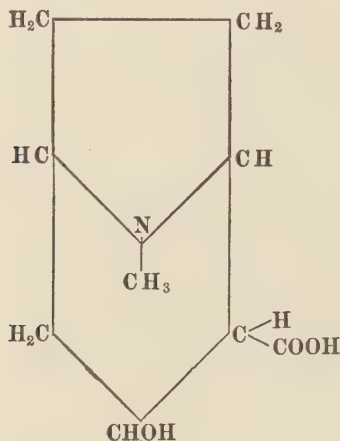
Eumydrine is the nitrate of methyl atropine, CH_3 and NO_3 attaching to the N atom of atropine, the latter changing its valence to five. It is used

for the same purposes as atropine, but is much less toxic.

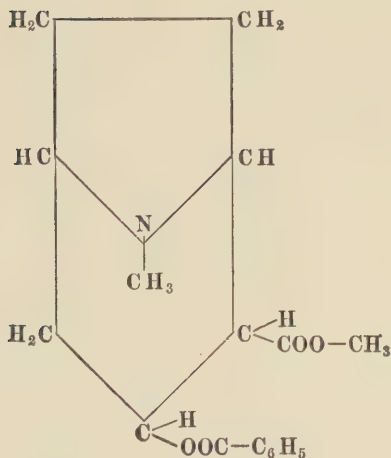
Homatropine is an artificial alkaloid prepared by the condensation of tropine and mandelic acid in ester combination. It dilates the pupil more promptly and less persistently than atropine.

Hyoscine and **scopolamine** are esters also, consisting of tropic acid combined with scopolin, $C_8H_{13}NO_2$, an alcohol derived from pyrrolidine. They are isomeric, hyoscine being lævorotatory and scopolamine racemic.

If in tropine an H atom of a CH_2 group of the secondary ring be replaced by $COOH$, ecgonine is obtained:



From this is derived **cocaine**, which is the methyl ester of ecgonine benzoate:



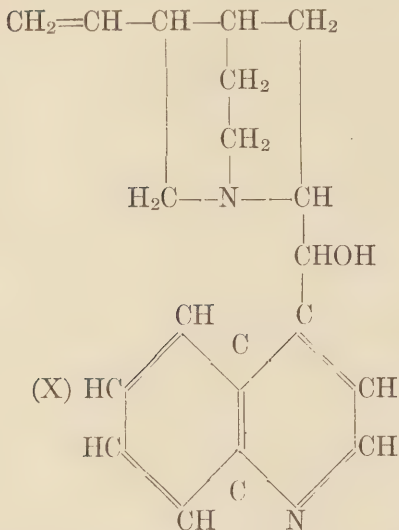
Cocaine exists both as *d* and as *l*, the latter having a more marked action. Cocaine is a very valuable local anæsthetic. Its solution cannot be sterilized by heat, because it hydrolyzes readily, yielding methyl alcohol and benzoylecgonine.

Besides this similarity of cocaine to atropine in chemical structure, there are some resemblances in pharmacological action.

Tropacocaine has a formula similar to cocaine, but having CH_2 instead of $\text{CH} \cdot \text{COOCH}_3$. It is less toxic and as strongly anæsthetic as cocaine. It has little effect on the pupil.

QUINOLINE DERIVATIVES.

The chief alkaloids of this class are the cinchona alkaloids. The following formula has been suggested for **cinchonine**:



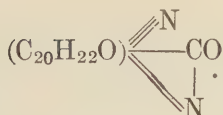
Quinine has the same formula, except that an H atom at the position marked (X) is replaced by the methoxy group (OCH_3).

Cinchonine is dextrorotatory, quinine lævorotatory. **Cinchonidine** is the lævorotatory isomer of cinchonine. **Quinidine** is the dextrorotatory isomer of quinine. Quinine is important as a medicine. It is very bitter.

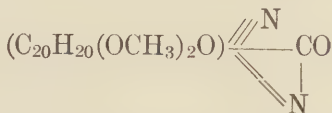
Euquinine, an ester, quinine ethyl carbonate, is tasteless. It gives full quinine action.

Quinine urea hydrochloride, a crystalline double salt, is very soluble and is suitable for subcutaneous injection, being non-irritating and even anæsthetic locally.

Strychnine and brucine are believed to be quinoline derivatives, but their structure has not been fully worked out. The nature of the nitrogen linkings is known. **Strychnine** may be represented as

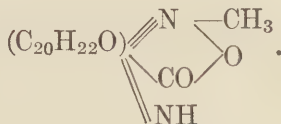


Brucine differs from it in having two methoxy (OCH_3) groups in the place of two-hydrogen atoms:



Both strychnine and brucine are lævorotatory. Strychnine is much used as a medicine, brucine not at all.

Methyl strychnine is obtained as follows: strychnine is treated with methyl iodide; an addition compound is formed, $\text{C}_{21}\text{H}_{22}\text{N}_2\text{O}_2 \cdot \text{ICH}_3$, the N atom which has the triple bond changing its valence from III to V in order to attach the I and CH_3 ; when this is treated with silver sulphate and barium hydroxide solution the product is the ammonium base, $\text{C}_{21}\text{H}_{22}\text{N}_2\text{O}_2 \cdot \text{CH}_3(\text{OH})$; on standing this becomes methyl strychnine,

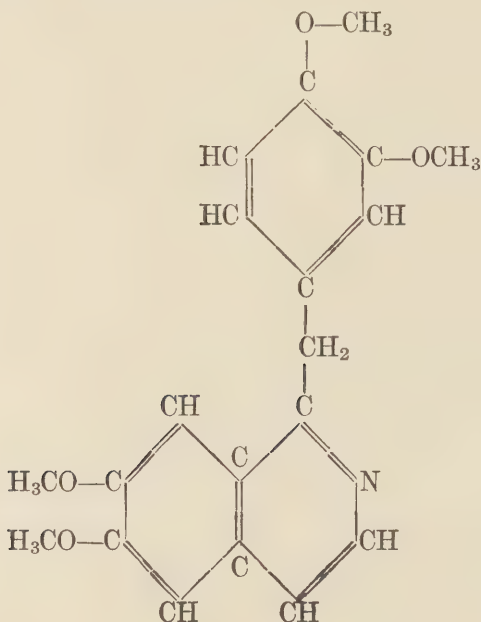


Dimethyl strychnine has the same formula, except that CH_3 is substituted for H in the NH group. This is produced from methyl strychnine in exactly the

same manner as the latter is derived from strychnine; in this case, however, no oxygen is introduced into the molecule, but only CH_3 .

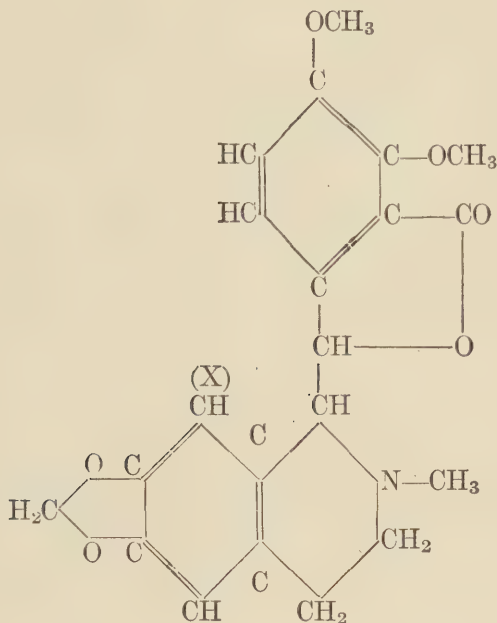
ISOQUINOLINE DERIVATIVES.

The *minor opium alkaloids*, papaverine, narcotine, and narceine, also *hydrastine* and *berberine*, belong to this group. These alkaloids are of very little importance (except hydrastine) therapeutically. **Papaverine** has the simplest structure; it is tetramethoxybenzylisoquinoline; its formula is



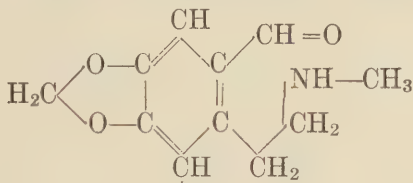
Papaverine has been synthesized.

Hydrastine has a similar but more complicated structure:



Narcotine is methoxyhydrastine, the OCH_3 group taking the place of H at (X).

Hydrastinine is an alkaloid prepared by oxidation of hydrastine with nitric acid. It has a much stronger physiological action than hydrastine. Its formula is



the side chain being bent so as to point out its derivation from hydrastine.

Narceine has a somewhat similar formula, but it has a benzoic acid group and several methoxy groups, additional.

Berberine has a still more complex formula.

Cotarnine, $C_{12}H_{15}NO_4$, is an oxidation product of narcotine, as hydrastinine is of hydrastine. Its formula corresponds to the isoquinoline half of the narcotine formula. Its hydrochloride is called **stypticin**, the phthalate is called **styptol**.

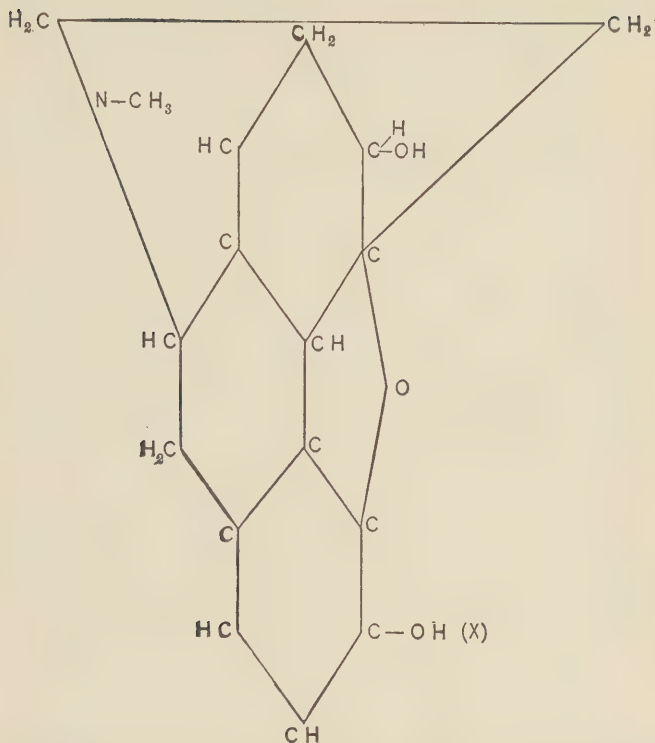
Cotarnine and hydrastinine have very similar physiological action; both affect the circulatory system in such a way as to lessen hæmorrhage. Cotarnine is much less expensive.

PHENANTHRENE DERIVATIVES.

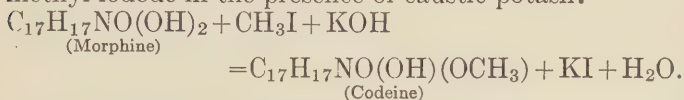
These are *morphine*, *codeine*, and *thebaine*, all of them being alkaloids present in opium. Derivatives of morphine artificially produced are apomorphine, dionine, heroine and peronine.

Morphine is the most valuable alkaloid for therapeutic purposes that we have. Opium contains about ten per cent of morphine. Its derivatives are much weaker in physiological action.

Its constitutional formula is now believed to be:



Codeine has the above formula, with CH_3 substituted for the H of the OH group at X. Thus codeine is the monomethyl ether of morphine. Codeine has been prepared from morphine by treating the latter with methyl iodide in the presence of caustic potash:

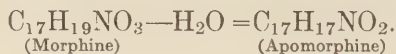


It is prepared commercially by heating a mixture of morphine and potassium methyl sulphate ($K(CH_3)SO_4$) with alcoholic KOH (see exp.).

Both morphine and codeine are lævorotatory.

Thebaine has two less hydrogen atoms attached to the phenanthrene nucleus, and has two OCH_3 groups in place of the two hydroxyls of morphine.

By the action of concentrated mineral acids, a molecule of water can be removed from morphine, producing **apomorphine**:

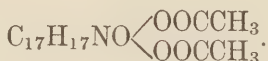


It is supposed that in apomorphine the phenanthrene nucleus is condensed with methyl piperidine. It turns green after long standing.

Other derivatives of morphine have been recently put forward as therapeutic agents.

Dionine is the hydrochloride of the ethyl ether of morphine, $\text{C}_{17}\text{H}_{17}\text{NO}(\text{OH})(\text{OC}_2\text{H}_5) \cdot \text{HCl}$.

Heroine is an ester, diacetate of morphine,



Peronine is the hydrochloride of the benzyl ether of morphine,



EXPERIMENTS. (1) Test solutions of morphine sulphate and quinine sulphate with alkaloidal reagents, as phosphomolybdic acid, mercuric potassium iodide, and tannic acid solutions.

(2) Dissolve quinine in dilute H_2SO_4 , notice the fluorescence.

(3) *Produce codeine.* Dissolve 1 gm. of morphine (pure alkaloid) and 0.6 gm. potassium methyl sulphate in 50 c.c. of pure methyl alcohol, warming and shaking. Then add an excess of powdered KOH until strongly alkaline, attach a reflux condenser and heat in a water bath for two hours. Add 20 c.c. of water, neutralize with HCl and distil off all volatile materials on a boiling water bath. Cool, make slightly alkaline with ammonia and filter, transfer to a separating funnel, and shake with several portions of benzene. Dry the combined benzene extracts with calcium chloride, filter into an evaporating dish, and evaporate to dryness on a water bath. Dissolve part of the residue with 2% HCl, warming gently.

Test a drop of the solution with potassium mercuric iodide solution. Also make the following tests: (a) make a paste of some ammonium molybdate with a few drops of C.P. H_2SO_4 , add a drop of the alkaloid solution—a blue colour is obtained; warm if necessary to develop the colour; (b) to a few drops of the solution add 2 c.c. of H_2SO_4 containing 1 drop of formaline—a reddish-violet colour. These two tests are given also by morphine, but morphine cannot be extracted by means of benzene. A test given by codeine, but not by morphine, is this: to the residue in the evaporating dish add about 1 c.c. of 20% H_2SO_4 and warm—a faint pink colour appears.

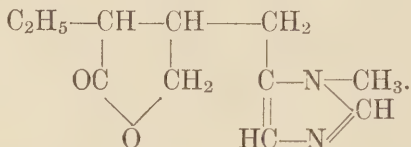
This method of synthesis should yield considerable impure codeine. Crystals can be obtained by dissolving a little in chloroform, and allowing a drop of the solution to evaporate on a slide.

PURIN DERIVATIVES.

The methyl xanthins, caffeine and theobromine, have been discussed elsewhere (p. 236).

Theophylline is 1, 3- dimethyl- 2, 6- dioxypurin, an isomer, therefore of theobromine. These three alkaloids can be prepared synthetically. All are used as remedies.

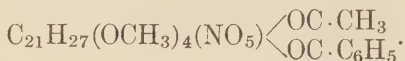
Pilocarpine does not have the full purin nucleus, its formula is



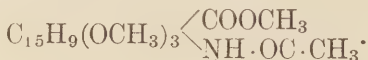
It is dextrorotatory. It has a marked pharmacological action.

CERTAIN ALKALOIDS THAT HAVE NOT BEEN CLASSIFIED.

The following indicates what is known about the structure of **aconitine**:



Colchicine is given the formula:



DRUG PRINCIPLES OF UNKNOWN STRUCTURE.

Cantharidin, $\text{C}_{10}\text{H}_{12}\text{O}_4$, is a lactone, derived from either benzene or cyclohexane.

Picrotoxin, $\text{C}_{15}\text{H}_{16}\text{O}_6$.

Picropodophyllin, $\text{C}_{72}\text{H}_{74}\text{O}_9 \cdot 2\text{H}_2\text{O}$.

APPENDIX.

Note to the Instructor.¹ If it is desired to shorten the time given to the experiments, we would advise omitting the following: preparation of phenol from potassium benzene sulphonate (see p. 341), the diazonium experiments (see p. 336), preparation of sulphanilic acid (see p. 357), of quinoline (see p. 379), and of codeine (see p. 398).

Diazonium salt may be prepared as a demonstration by the instructor.

To permit of using one apparatus (as a Beckmann apparatus or a combustion furnace) with the entire class, we would suggest dividing the class or a section of it into five groups of three or four men each, the men of each group working together on a particular experiment, but the various groups performing different experiments on the same day. For example, one group

¹ We can recommend as valuable books for reference the text-books of organic chemistry by Remsen, Holleman, W. A. Noyes, Bernthsen, and Meyer and Jacobson, the laboratory manuals by Gattermann (translated by Schober), W. A. Noyes (2d edition), and Cohen, and "Introduction to Physical Chemistry," by Walker.

periments on the same day. For example, one group may do crystallization and melting-point experiments (see pp. 9, 10), a second may carry out fractional distillation (see p. 13) and boiling-point determination (see p. 17), a third may make specific gravity determinations (see p. 22), a fourth may do a combustion analysis (see p. 29), and a fifth may use the Beckmann apparatus (see p. 55). Each group will, of course, have to take the experiments in a different order, thus:

Group	I,	Lessons	1, 2, 3, 4, 5.
"	II,	"	2, 3, 4, 5, 1.
"	III,	"	3, 4, 5, 1, 2.
"	IV,	"	4, 5, 1, 2, 3.
"	V,	"	5, 1, 2, 3, 4.

Spellings. We have retained the ending "ine" in the case of amines and alkaloids, with the idea of indicating by this means the organic substances that are *distinctly basic* in character.

Formulae. We strongly advise that the learning of empirical formulæ by the student be discouraged, but that, on the other hand, the student be thoroughly drilled in giving structural formulæ.

REFERENCE TABLES.

TABLE I.

SPECIFIC GRAVITY AND PERCENTAGE OF ALCOHOL.

[According to Squibb.]

Per Cent Alcohol by Volume.	Per Cent Alcohol by Weight.	Specific Gravity.		Per Cent Alcohol by Volume.	Per Cent Alcohol by Weight.	Specific Gravity.	
		At 15.56° C.	At 25° C.			At 15.56° C.	At 25° C.
1	0.79	0.9985	0.9970	31	25.51	0.9643	0.9594
2	1.59	.9970	.9953	32	26.37	.9631	.9582
3	2.39	.9956	.9938	33	27.23	.9618	.9567
4	3.20	.9942	.9922	34	28.09	.9609	.9556
5	4.00	.9930	.9909	35	28.96	.9593	.9538
6	4.80	.9914	.9893	36	29.83	.9578	.9521
7	5.61	.9898	.9876	37	30.70	.9565	.9507
8	6.42	.9890	.9868	38	31.58	.9550	.9489
9	7.23	.9878	.9855	39	32.46	.9535	.9473
10	8.04	.9869	.9846	40	33.35	.9519	.9456
11	8.86	.9855	.9831	41	34.24	.9503	.9438
12	9.67	.9841	.9816	42	35.13	.9490	.9424
13	10.49	.9828	.9801	43	36.03	.9470	.9402
14	11.31	.9821	.9793	44	36.93	.9452	.9382
15	12.13	.9815	.9787	45	37.84	.9434	.9363
16	12.95	.9802	.9773	46	38.75	.9416	.9343
17	13.78	.9789	.9759	47	39.67	.9396	.9323
18	14.60	.9778	.9746	48	40.60	.9381	.9307
19	15.43	.9766	.9733	49	41.52	.9362	.9288
20	16.26	.9760	.9726	50	42.52	.9343	.9267
21	17.09	.9753	.9719	51	43.47	.9323	.9246
22	17.92	.9741	.9706	52	44.42	.9303	.9226
23	18.76	.9728	.9692	53	45.36	.9283	.9205
24	19.59	.9716	.9678	54	46.32	.9262	.9184
25	20.43	.9709	.9668	55	47.29	.9242	.9164
26	21.27	.9698	.9655	56	48.26	.9221	.9143
27	22.11	.9691	.9646	57	49.23	.9200	.9122
28	22.96	.9678	.9631	58	50.21	.9178	.9100
29	23.81	.9665	.9617	59	51.20	.9160	.9081
30	24.66	.9652	.9603	60	52.20	.9135	.9056

TABLE I—*Continued*

[According to Squibb.]

Per Cent Alcohol by Volume.	Per Cent Alcohol by Weight.	Specific Gravity.		Per Cent Alcohol by Volume.	Per Cent Alcohol by Weight.	Specific Gravity.	
		At 15.56° C.	At 25° C.			At 15.56° C.	At 25° C.
61	53.20	0.9113	0.9034	81	74.74	0.8611	0.8530
62	54.21	.9090	.9011	82	75.91	.8581	.8500
63	55.21	.9069	.8989	83	77.09	.8557	.8476
64	56.22	.9047	.8969	84	78.29	.8526	.8444
65	57.20	.9025	.8947	85	79.50	.8496	.8414
66	58.27	.9001	.8923	86	80.71	.8466	.8384
67	59.32	.8973	.8895	87	81.94	.8434	.8352
68	60.38	.8949	.8870	88	83.19	.8408	.8326
69	61.42	.8925	.8846	89	84.46	.8373	.8291
70	62.50	.8900	.8821	90	85.75	.8340	.8258
71	63.58	.8875	.8796	91	87.00	.8305	.8223
72	64.66	.8850	.8771	92	88.37	.8272	.8191
73	65.74	.8825	.8746	93	89.71	.8237	.8156
74	66.83	.8799	.8719	94	91.07	.8199	.8118
75	67.93	.8769	.8689	95	92.46	.8164	.8083
76	69.05	.8745	.8665	96	93.89	.8125	.8044
77	70.18	.8721	.8641	97	95.34	.8084	.8003
78	71.31	.8696	.8616	98	96.84	.8041	.7960
79	72.45	.8664	.8583	99	98.39	.7995	.7914
80	73.59	.8639	.8558	100	100.00	.7946	.7865

The table of the U. S. Bureau of Standards gives specific gravities for a number of concentrations of alcohol differing from those in this table by 0.0002 to 0.0005, for instance, the figures for 95–100% alcohol are lower by 0.0004–0.0006.

TABLE II.

WEIGHT OF PURE NITROGEN IN MILLIGRAMS IN 1 C.C. OF THE
MOIST GAS AT VARIOUS TEMPERATURES AND UNDER VARIOUS
PRESSURES (MILLIMETRES OF MERCURY).

Tem- perature.	721	724	727	730	733	736	739	742
10	1.130	1.135	1.139	1.144	1.149	1.154	1.158	1.163
11	1.125	1.129	1.134	1.139	1.144	1.148	1.153	1.158
12	1.120	1.124	1.129	1.134	1.139	1.143	1.148	1.153
13	1.115	1.119	1.124	1.129	1.134	1.138	1.143	1.148
14	1.110	1.114	1.119	1.124	1.129	1.133	1.138	1.143
15	1.105	1.109	1.114	1.119	1.124	1.128	1.133	1.138
16	1.099	1.103	1.108	1.113	1.118	1.123	1.127	1.132
17	1.094	1.098	1.103	1.108	1.113	1.118	1.122	1.127
18	1.089	1.093	1.098	1.102	1.107	1.112	1.116	1.121
19	1.084	1.088	1.093	1.097	1.102	1.107	1.111	1.116
20	1.079	1.083	1.088	1.092	1.097	1.102	1.106	1.111
21	1.074	1.078	1.082	1.087	1.091	1.096	1.101	1.106
22	1.068	1.072	1.076	1.081	1.086	1.091	1.095	1.100
23	1.062	1.067	1.071	1.076	1.080	1.085	1.090	1.094
24	1.057	1.061	1.066	1.071	1.075	1.080	1.084	1.089
25	1.051	1.056	1.060	1.065	1.069	1.074	1.078	1.083
26	1.046	1.050	1.054	1.059	1.064	1.068	1.072	1.077
27	1.040	1.044	1.048	1.053	1.058	1.062	1.066	1.071
28	1.034	1.038	1.042	1.047	1.052	1.056	1.060	1.065
29	1.028	1.032	1.036	1.041	1.046	1.050	1.054	1.059
30	1.022	1.026	1.031	1.035	1.040	1.044	1.048	1.053

Tem- perature.	745	748	751	754	757	760	763	766
10°	1.168	1.173	1.177	1.182	1.187	1.192	1.197	1.202
11	1.162	1.167	1.172	1.176	1.181	1.186	1.191	1.196
12	1.157	1.162	1.167	1.171	1.176	1.181	1.186	1.190
13	1.152	1.157	1.162	1.166	1.171	1.176	1.181	1.185
14	1.147	1.152	1.157	1.161	1.166	1.171	1.176	1.180
15	1.142	1.147	1.152	1.156	1.161	1.166	1.170	1.175
16	1.137	1.141	1.146	1.150	1.155	1.160	1.164	1.169
17	1.131	1.136	1.140	1.144	1.149	1.154	1.158	1.163
18	1.125	1.130	1.135	1.139	1.144	1.149	1.153	1.158
19	1.120	1.125	1.130	1.134	1.139	1.144	1.148	1.153
20	1.115	1.120	1.125	1.129	1.134	1.138	1.143	1.148
21	1.110	1.114	1.119	1.123	1.128	1.133	1.138	1.142
22	1.104	1.108	1.113	1.117	1.122	1.127	1.132	1.136
23	1.098	1.103	1.107	1.111	1.116	1.121	1.126	1.131
24	1.093	1.097	1.101	1.106	1.111	1.116	1.121	1.125
25	1.087	1.092	1.096	1.101	1.105	1.110	1.115	1.119
26	1.082	1.086	1.090	1.095	1.099	1.104	1.108	1.113
27	1.076	1.080	1.084	1.089	1.093	1.098	1.102	1.107
28	1.070	1.074	1.078	1.083	1.087	1.092	1.096	1.101
29	1.063	1.068	1.072	1.077	1.081	1.086	1.090	1.095
30	1.057	1.062	1.066	1.071	1.075	1.080	1.084	1.089

TABLE III.

SPECIFIC GRAVITY AND PERCENTAGE OF NaOH IN AQUEOUS SOLUTION.

Specific Gravity at 15°.	Per Cent NaOH.	Gm. NaOH in 100 c.c.	Specific Gravity at 15°.	Per Cent NaOH.	Gm. NaOH in 100 c.c.
1.007	0.61	0.6	1.220	19.58	23.9
1.014	1.20	1.2	1.231	20.59	25.3
1.022	2.00	2.1	1.241	21.42	26.6
1.029	2.71	2.8	1.252	22.64	28.3
1.036	3.35	3.5	1.263	23.67	29.9
1.045	4.00	4.2	1.274	24.81	31.6
1.052	4.64	4.9	1.285	25.80	33.2
1.060	5.29	5.6	1.297	26.83	34.8
1.067	5.87	6.3	1.308	27.83	36.4
1.075	6.55	7.0	1.320	28.83	38.1
1.083	7.31	7.9	1.332	29.93	39.9
1.091	8.00	8.7	1.345	31.22	42.0
1.100	8.68	9.5	1.357	32.47	44.1
1.108	9.42	10.4	1.370	33.69	46.2
1.116	10.06	11.2	1.384	34.96	48.3
1.125	10.97	12.3	1.397	36.25	50.6
1.134	11.84	13.4	1.410	37.47	52.8
1.142	12.64	14.4	1.424	38.80	55.3
1.152	13.55	15.6	1.438	39.99	57.5
1.162	14.37	16.7	1.453	41.41	60.2
1.171	15.13	17.7	1.468	42.83	62.9
1.180	15.91	18.8	1.483	44.38	65.8
1.190	16.77	20.0	1.498	46.15	69.1
1.200	17.67	21.2	1.514	47.60	72.1
1.210	18.58	22.5	1.530	49.02	75.0

TABLE IV.

SPECIFIC GRAVITY AND PERCENTAGE OF KOH IN AQUEOUS SOLUTION.

Specific Gravity at 15°.	Per Cent KOH.	Gm. KOH in 100 c.c.	Specific Gravity at 15°.	Per Cent KOH.	Gm. KOH in 100 c.c.
1.007	0.9	0.9	1.252	27.0	33.8
1.014	1.7	1.7	1.263	28.0	35.3
1.022	2.6	2.6	1.274	28.9	36.8
1.029	3.5	3.6	1.285	29.8	38.5
1.037	4.5	4.6	1.297	30.7	39.8
1.045	5.6	5.8	1.308	31.8	41.6
1.052	6.4	6.7	1.320	32.7	43.2
1.060	7.4	7.8	1.332	33.7	44.9
1.067	8.2	8.8	1.345	34.9	46.9
1.075	9.2	9.9	1.357	35.9	48.7
1.083	10.1	10.9	1.370	36.9	50.6
1.091	10.9	11.9	1.383	37.8	52.2
1.100	12.0	13.2	1.397	38.9	54.3
1.108	12.9	14.3	1.410	39.9	56.3
1.116	13.8	15.3	1.424	40.9	58.2
1.125	14.8	16.7	1.438	42.1	60.5
1.134	15.7	17.8	1.453	43.4	63.1
1.142	16.5	18.8	1.468	44.6	65.5
1.152	17.6	20.3	1.483	45.8	67.9
1.162	18.6	21.6	1.498	47.1	70.6
1.171	19.5	22.8	1.514	48.3	73.1
1.180	20.5	24.2	1.530	49.4	75.6
1.190	21.4	25.5	1.546	50.6	77.9
1.200	22.4	26.9	1.563	51.9	81.1
1.210	23.3	28.2	1.580	53.2	84.0
1.220	24.2	29.5	1.597	54.5	87.0
1.231	25.1	30.9	1.615	55.9	90.2
1.241	26.1	32.4	1.634	57.5	94.0

TABLE V.
ACETIC ACID.

Specific Gravity at 15° of Various Concentrations.				Freezing-point, as Affected by Water-content.			
Per Cent of Acetic Acid.	Specific Gravity	Per Cent of Acetic Acid.	Specific Gravity	Per Cent of Water.	Freez- ing- point.	Per Cent of Water.	Freez- ing- point.
10.0	1.014	60.0	1.069	1.0	14.8°	5.6	8.2°
20.0	1.028	70.0	1.073	2.0	13.25	6.5	7.1
30.0	1.041	80.0	1.075	2.9	11.95	8.3	5.3
40.0	1.052	90.0	1.071	3.8	10.5	9.1	4.3
50.0	1.062	100.0	1.055	4.8	9.4	9.9	3.6

TABLE VI.

VAPOUR TENSION (AQUEOUS PRESSURE IN MILLIMETERS OF MERCURY) OF WATER AND OF 40% KOH AT VARIOUS TEMPERATURES.

Tem- perature	Pure H ₂ O.	40% KOH.	Tem- perature	Pure H ₂ O.	40% KOH.	Tem- perature	Pure H ₂ O.	40% KOH.
0	4.6	2.6	12	10.5	5.8	24	22.2	11.7
1	4.9	2.8	13	11.2	6.1	25	23.5	12.4
2	5.3	3.0	14	11.9	6.5	26	25.0	13.1
3	5.7	3.2	15	12.7	6.9	27	26.5	13.8
4	6.1	3.4	16	13.6	7.4	28	28.1	14.7
5	6.5	3.6	17	14.4	7.8	29	29.8	15.5
6	7.0	3.9	18	15.4	8.3	30	31.6	16.4
7	7.5	4.1	19	16.4	8.9	31	33.4	17.3
8	8.0	4.4	20	17.4	9.3	32	35.4	18.3
9	8.6	4.7	21	18.5	9.9	33	37.4	19.4
10	9.2	5.1	22	19.7	10.5	34	39.6	20.5
11	9.8	5.4	23	20.9	11.1	35	41.9	21.5

TABLE VII.

THE DISSOCIATION CONSTANTS OF CERTAIN WEAK ACIDS.

Substance.	100K.	Substance.	100K.
Formic	0.02140	β -Hydroxypropionic	0.00311
Acetic	0.00180	Lactic	0.0138
Propionic	0.00145	Glyceric	0.0228
Butyric	0.00175	Malonic	0.163
Valerianic	0.00156	Succinic	0.00665
Caproic	0.00147	Glutaric	0.00475
Monochloracetic	0.155	Tartaric	0.097
Dichloracetic	5.144	Benzoic	0.006
Trichloracetic	120.00	<i>o</i> -Hydroxybenzoic,	
Monobromacetic	0.138	salicylic	0.102
Cyanacetic	0.370	<i>m</i> -Hydroxybenzoic .	0.0087
Glycollic	0.0152	<i>p</i> -Hydroxybenzoic .	0.0029
		Phenol	0.000000013

TABLE VIII.

DISSOCIATION CONSTANTS OF CERTAIN BASES.

Substance.	100K.	Substance.	100K.
Ammonia	0.0023	Diethylamine	0.126
Methylamine	0.050	Trimethylamine	0.0074
Ethylamine	0.056	Triethylamine	0.064
Dimethylamine	0.074	Benzylamine	0.0024

TABLE IX.

THE POWER OF CERTAIN ACIDS TO CAUSE HYDROLYSIS.

Acid.	Inversion Coefficients (Cane-sugar).	Velocity Coefficients (Methylace- tate).	Velocity Coefficients (Acetamide).
Hydrochloric acid.....	1.000	1.000	1.000
Nitric acid.....	1.000	0.915	0.955
Hydrobromic acid.....	1.114	0.983	0.972
Sulphuric acid.....	0.536	0.541	0.547
Formic acid.....	0.0153	0.0131	0.00532
Acetic acid.....	0.0040	0.00345	0.000747
Monochloracetic acid.....	0.0484	0.0430	0.0295
Dichloracetic acid.....	0.271	0.2304	0.245
Trichloracetic acid.....	0.754	0.6820	0.670
Oxalic acid.....	0.1857	0.1746	0.169
Succinic acid.....	0.00545	0.00496	0.00195
Citric acid.....	0.0172	0.01635	0.00797

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